

Protocol Information

Protocol title	Evaluation of the Clinical Impact and Safety of Focused Transesophageal Echocardiography During Resuscitation of Critically Ill Patients in the Emergency Department and Intensive Care Settings
Short Title	Focused TEE in Critically-ill patients
Brief description of the protocol	The general objective of this study is to evaluate the clinical impact and safety of transesophageal echocardiography (TEE) used during the evaluation of critically-ill patients in the emergency and intensive care settings. The target population for this study are critically-ill patients over the age of 18 who as part of their routine clinical care are receiving a focused TEE. There are no interventions, outside those that represent standard clinical care, as part of this study.
Resubmission*	No
Application type	EXPEDITED Category 5
Approval and Expiration	Approval: November 24, 2020 Expiration: December 1, 2021 *Intention to request extension of approval

Overall objectives

The primary objective of this study is to determine the **clinical impact** and **safety** of transesophageal echocardiography (TEE) performed during the evaluation of critically-ill patients in the **emergency department** and **intensive care settings**.

The secondary objective(s) of this study are to **characterize the use of this imaging modality** in the subsets of critically-ill patients in **shock and cardiac arrest**; including but not limited to; description of the frequency of studies, clinical indications, clinician characteristics, echocardiography findings, timing of studies, procedure-related complications and patient outcomes.

Background

Goal-directed transesophageal echocardiography (TEE) is frequently used by physicians caring for intubated critically-ill patients as a reliable imaging modality that is well-suited to answer questions at bedside.

While in most patients, transthoracic echocardiography (TTE) can provide the information needed, there are situations in which goal-directed transesophageal echocardiography (TEE) provides superior diagnostic value. In contrast with comprehensive echocardiography, TEE

provides acute care clinicians with a goal-directed framework to guide clinical care at the point-of-care in various clinical scenarios. Common applications of TEE in critically-ill patients include assessment of circulatory failure, hemodynamic monitoring, evaluation of unexplained hypoxemia, procedural guidance and cardiac arrest.

Over the last decade, a small number of studies have demonstrated the feasibility and clinical impact of TEE in different acute care settings, including the emergency department and intensive care units.

In both of these settings, **retrospective studies** of focused TEE have demonstrated this modality to be clinically impactful in the diagnostic evaluation of patients in shock, hemodynamic monitoring in patients with circulatory failure, in the evaluation of fluid responsiveness to guide fluid therapy, and in the guidance of procedures such as percutaneous mechanical circulatory support.

Specifically in the emergency department setting, one small prospective observational study evaluating the use of TEE during resuscitation, has shown that traditional chest compressions following external landmarks as recommended by guidelines, resulted in an AMC located over the ascending thoracic aorta, or left ventricular outflow tract in over 50% of patients, suggesting that compressions over the center of the heart may actually impede some of the potential forward blood flow in a significant portion of patients. Most recently animal models of cardiac arrest have demonstrated that chest compressions performed directly over the LV rather than the center of the chest result in improved aortic pressures, ETCO₂, and survival.

While the above-mentioned studies have provided some promising data on the utility of this emerging modality, to date only small single center and retrospective studies have evaluated the clinical impact of focused TEE in resuscitative settings. Furthermore, no studies have investigated the safety of this imaging modality, specifically in the population of emergency department patients. The proposed study has the potential to substantially improve our understanding of the clinical impact and the safety of TEE in emergency and critical care applications.

Study Design

Design

We plan to conduct a prospective observational study involving a convenient sample of patients receiving a TEE as part of their clinical care in emergency department (ED) and intensive care unit (ICU) settings. The study will enroll adult patients receiving focused TEE as part of their routine care for the most common clinical indications of focused TEE in critical care patients in ED and ICU settings including: 1. **Evaluation of intra-arrest and post cardiac arrest in in-hospital (IHCA) and out-of-hospital cardiac arrest (OHCA)**, 2. **Evaluation of patients in shock**, 3. **Hemodynamic monitoring**, and 4. **Procedural guidance**.

Data will be collected from the patients' electronic medical record (EMR) and EMS run-sheets in the case of OHCA cases. Transesophageal echocardiography (TEE) images routinely recorded for quality assurance and as part of standard clinical care, will be collected. Patients will be

enrolled in the study by clinicians participating from their care who are involved in the performance of TEE. Following identification of eligibility criteria by the enrolling clinician, a RedCap data collection instrument will be used to prospectively gather basic demographics, and clinical data, including the indication for the TEE (i.e. including intra-arrest or post arrest, evaluation of shock, hemodynamic monitoring or procedural guidance), operator findings on the TEE, probe insertion procedure details, TEE views obtained during the study, clinician's interpretation of the images, change in management (if any) as a result of the information provided by TEE. Procedure-related immediate complications, and outcomes when indicated.

Minimal patient demographic information to be collected including: age, gender, and BMI. In the case of cardiac arrests, when applicable the following information will be collected: if the arrest was witnessed, location of arrest, if bystander CPR was performed, will be obtained from the EMR and EMS run sheets. Identification of certain disease states in the medical history patients such as coronary artery disease, congestive heart failure, chronic kidney disease, diabetes mellitus, hypertension, previous STEMI, ventricular assist device, and implantable cardioverter-defibrillator will also be obtained from the EMR and prospectively entered to the RedCap data form. For cases of OHCA, data collection will also include an analysis of pre-hospital care to examine the following factors (Ustein Cardiac Arrest Variables); estimated time of arrest, response time, EMS interventions (chest compressions, defibrillation, airway procedures, dosing and timing of drug administration). For all cardiac arrest cases, information collected will also include time of arrest, ED arrival time in case of OHCA, time to first image of TEE, time of first rhythm, and times and type of intervention (mechanical CPR, arterial line, epi administration, etc.) The study of patient outcomes will be specific to the clinical indication and will include ROSC, survival to hospitalization and discharge in OHCA. In cardiac arrest cases, additional factors pertaining CPR physiology will be examined.

Study duration

The expected duration of the study is 1 year. The relevant dates are data collected from December 1st, 2020 to December 1st, 2021.

Target population

Adult patients who as part of their routine clinical care receive focused TEE in the emergency department of intensive care setting. Children (age under 18 years) will not be eligible for inclusion in this study.

Subjects enrolled by Penn Researchers

Subjects enrolled by Collaborating Researchers

N/A

Vulnerable Populations*

None of the above populations are included in the research study

Subject recruitment*

Not applicable

Subject compensation*

No

Procedures

There are no interventions or procedures in this study. As part of this study, we are not proposing any manipulation to the subject's clinical environment, therefore any procedures or surgical interventions that take place during the clinical encounter in which TEE is being performed, are being performed as part of standard clinical care and in the interest of the patient rather than for study purposes.

We will be entering previously described clinical data into REDCap from EPIC patient charts. The TEE ultrasound clips that are routinely stored for quality assurance will be reviewed, analyzed, and qualitative data will be extracted. All of the data will be analyzed retrospectively from standard of care procedures. Follow-up, beyond hospital discharge of subjects will not occur.

Deception

No

Analysis Plan

Baseline and demographic characteristics will be summarized by standard descriptive statistics (including mean and standard deviation for continuous variables such as age and standard percentages for categorical variables such as gender). Continuous variables will be analyzed using Student's t-test, categorical data using Chi-square. Descriptive statistics will be presented as a mean with standard deviation, or as a median with an interquartile range. Differences in patient characteristics will be analyzed using χ^2 testing, Student's t-test, or the Mann-Whitney U test, as appropriate. We will provide frequencies with their binomial 95% confidence intervals for descriptive purposes. For bivariate or multivariable analyses, we will use logistic regression, ANOVA, or chi-squared testing, as appropriate. Statistical methods will be performed in statistical software (STATA).

Sample size:

Consistent with the descriptive nature of this study, our intention is to capture as many TEEs as possible within those performed across the clinical indications of interest for this study. Based on

prior research and Quality Assurance data, over the period of one year, we estimate a total of approximately 100 studies to be performed and analyzed as part of this study.

Subject Confidentiality

The long-range plan for protecting the confidentiality of research data, including a schedule for destruction of identifiers associated with the data.

Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.

Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.

Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.

Wherever feasible, identifiers will be removed from study-related information.

A waiver of documentation of consent is being requested, because the only link between the subject and the study would be the consent document and the primary risk is a breach of confidentiality. (This is not an option for FDA-regulated research.)

Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys.

REDCap, as an encrypted program, will be used to store all study variables and extracted data points.

Sensitive Research Information*

No

Data Disclosure

Protected Health Information/Data Protection*

Consent Process

Not Applicable

Potential Study Risks

Given the design as an observational protocol, there are no interventions as part of this study. As explained before, all the interventions such as procedures occurring during this protocol are the standard clinical practice and their use will be directed by the treating physicians as part of the standard care.

Radioisotopes/radiation-producing machines (e.g., X-rays, CT scans, fluoroscopy) and associated risks: No radioisotopes or radiation-producing machines will be used during the protocol.

Physical well-being: Participation in this study will not incur any additional risk to subjects' physical well being beyond what would be experienced during standard care. Psychological well-being: Participation in this study will not incur any additional risk to subjects' psychological well being beyond what would be experienced during standard care. Economic well-being. Participation in this study will not incur any additional risk to subjects' economic well being beyond what would be experienced during standard care. Social well-being. Participation in this study will not incur any additional risk to subjects' social well being beyond what would be experienced during standard care. Although the risk of mortality in our patient population is high (approximately 90%), the risk of the observations made in this study are minimal as all observations are currently being recorded as part of standard of care. All laptops, desktops, and mobile devices used to access, transmit, or store Prohibited or Restricted Data as defined under the Data Classification Guidelines are encrypted. We will make sure that any new device used in this study will be encrypted prior to use.

Potential Study Benefits

There will be no direct benefit to patients enrolled in this study. However, the knowledge gained from this research and specifically the greater understanding on the clinical impact and potential to improve outcomes of TEE in the care of critically-ill patients, will contribute greatly to the field and society at large.

Among other applications, this knowledge may contribute to the creation of guidelines for physicians that use this emerging ultrasound modality when caring for critically-ill patients, and may ultimately save patients from death and other adverse outcomes. The medical community's increased understanding of the value of this imaging modality and best practices in its use for patients with specific clinical conditions such as shock and cardiac arrest is also likely to result from this study.

Risk / Benefit Assessment

Minimal Risk