Official Title of the study:

Emergency Physician Performed Resuscitative Transesophageal Echocardiography (TEE) To Diagnose Blunt Traumatic Aortic Injury (BTAI)

Date of Document:

22rd February 2022

Study Title

Emergency Physician Performed Resuscitative Transesophageal Echocardiography (TEE) To Diagnose Blunt Traumatic Aortic Injury (BTAI)

Study type

Multicentre prospective observational study

Primary Investigator

Dr. Adi Bin Osman
Consultant Emergency Medicine
Emergency and Trauma Department
Hospital Raja Permaisuri Bainun
Jalan Raja Ashman Shah, 30450 Ipoh, Perak.
osman.adi@gmail.com

Co-Investigator

Dr. Chan Pei Fong
Emergency Physician
Emergency and Trauma Department
Hospital Raja Permaisuri Bainun
Jalan Raja Ashman Shah, 30450 Ipoh, Perak.
chanpeifong@yahoo.com

Dr. Azma Haryaty Ahmad,
Emergency Physician
Emergency and Trauma Department
Hospital Raja Permaisuri Bainun
Jalan Raja Ashman Shah, 30450 Ipoh, Perak.
drazma78@yahoo.com.my

Assoc. Prof. Dr. Shaik Farid Abdull Wahab
Head of Department of Emergency Medicine,
School of Medical Sciences, Health Campus,
Universiti Sains Malaysia,
16150 Kubang Kerian, Kelantan, Malaysia
drsfarid@usm.my

Dr. Roslanuddin bin Mohd Salehuddin
Emergency and Trauma Department
Hospital Sultanah Bahiyah,
Km 6, Jalan Langgar, 05460, Alor Setar
sledgy04@yahoo.com

Dr Sri Rao Siva
Emergency & Trauma Department
Hospital Kuala Lumpur
Jalan Pahang, Wilayah Persekutuan 50586, Kuala Lumpur
Malaysia
sriraosiva@gmail.com

Mohd Hafis B Mohamed Sakan
Emergency and Trauma Department
Hospital Melaka
Jln Mufti Haji Khalil
75400 Melaka
hafissakan@gmail.com

Muhammad Yusuf bin Muharam
Emergency & Trauma Department
Queen Elizabeth Hospital
Karung Berkunci 2029,
88586, Kota Kinabalu, Sabah.
drmdyusuf@moh.gov.my

Study Site

1. Emergency and Trauma Department
Hospital Raja Permaisuri Bainun, Ipoh, Perak.

2. Department of Emergency Medicine,
School of Medical Sciences, Health Campus,
Universiti Sains Malaysia, Kelantan.

3. Emergency and Trauma Department
Hospital Sultanah Bahiyah, Alor Setar, Kedah

4. Emergency & Trauma Department
Hospital Kuala Lumpur, Kuala Lumpur.

5. Emergency and Trauma Department
Hospital Melaka, Melaka

6. Emergency & Trauma Department
Queen Elizabeth Hospital
Kota Kinabalu, Sabah.

List of Abbreviations

TEE	transesophageal echocardiography
BTAI	blunt traumatic aortic injury
ED	emergency department
CTA	computed tomography angiography
EFAST	extended focused assessment with sonography for trauma
TREE	trauma resuscitation transesophagal echocardiography

Research Synopsis

Study title	Emergency Physician Performed ResuscitativeTransesophageal Echocardiography (TEE) to Diagnose Blunt Traumatic Aortic Injury (BTAI)
Study Population	All trauma patients with suspected BTAI at the emergency department (ED)
Study Design	Multicentre prospective observational study
Objective	To determine test performance of resuscitative transesophageal echocardiography performed by emergency physician ultrasound for the identification of blunt traumatic aortic injury
Study endpoints/outcomes	Primary endpoints: Sensitivity and specificity of resuscitative TEE in identification of BTAI in comparison to CTA.
Sample Size	56
Study Duration	15-03-2022 until 15-3-2023

1. Background and Significance

Blunt traumatic aortic injury (BTAI) is the second most common cause of death in blunt trauma with 80% of the patients dying at the scene (1, 2). The remaining survivors have an in-hospital of about 50% (2). It is thus important to diagnose BTAI as soon as possible to maximize the window of opportunity for definite treatment (3).

Traditionally, invasive catheter aortography used to be the investigation of choice in diagnosing BTAI (4). With the introduction of helical computed tomography (CT) followed by CT angiography (CTA) in the 1990s (5), CT scan became the acceptable gold standard due to its high sensitivity of 96-100% and specificity of 95.0-99.8% (2,6).

For patients who are hemodynamically unstable to be transported to CT suite, transesophageal echocardiography has been shown to be a reasonable alternative in identification of BTAI (7,8,9). Similar to the use of transthoracic ultrasound in extended focused assessment with sonography for trauma (EFAST), trauma resuscitation transesophagal echocardiography (TREE) is a rapid bedside tool to assess the patient and guide potential therapy when transthoracic ultrasound is not possible (10,11). In fact, TEE has been proven to be more accurate in severe chest trauma compare to transthoracic echocardiography to pick up life-threatening injuries (12).

Many studies had compared TEE with CT scan in the evaluation of aorta in the non-trauma setting. CTA has been proven to be more superior to TEE to evaluate the atherosclerotic aorta in stroke (13). A meta-analysis in 2006 by Shiga et al showed that TEE and helical CT chest has similar positive likelihood ratio of 14.1 and 13.9 respectively in comparison to MRI (25.3) when diagnosing suspected thoracic aortic dissection (9).

The accuracy of TEE and helical chest CT in diagnosing BTAI were validated against aortography separately in previous studies (7,9,14,15). Cinnella compared both imaging in an article review in 1998 in evaluating BTAI but did not find superiority in either helical chest CT or TEE (16). There was only one study which made a head-to- head comparison between helical chest CT with TEE in 2001 by Vignon et al in diagnosing BTAI. It was found that both modalities showed similar diagnostic accuracy with 100% specificity in diagnosing acute aortic injury (8). However, TEE was found to be more sensitive (93%) than helical chest CT (73%) in identifying thoracic aorta injuries especially intimal and medial lesions.

To date, there is no study comparing CTA and TEE by emergency physicians to diagnose BTAI. Here we will like to determine to test performance of resuscitative transesophageal echocardiography performed by emergency physician ultrasound for the identification of BTAI in chest trauma.

2. Objective

The objective of this study is to determine test performance of resuscitative transesophageal echocardiography performed by emergency physician ultrasound for the identification of blunt traumatic aortic injury.

Primary endpoints: Sensitivity and specificity of resuscitative TEE in identification of BTAI, in comparison to CTA.

3. Methodology

3.1 Study Type and Design

This is a multicentre prospective observational trial. All trauma patients with suspected BTAI at the emergency department (ED) will undergo resuscitative transesophageal echocardiography to evaluate the thoracic aorta.

Resuscitative TEE is a minimally invasive procedure to evaluate all chest trauma patients. Besides the aorta, TEE can also provide other useful information regarding the hemodynamic status, cardiac function and lung pathology of the patient.

Patients will be recruited into the study by investigators who take informed consent from the patient or next of kin prior to the TEE procedure.

For all patients with suspected BTAI, CTA is mandatory to confirm the diagnosis of BTAI.

TEE findings of BTAI will be compared to CTA which will be considered the reference standard unless confirmation is available from surgical procedures or autopsy.

Inter-observer variability for normal or pathological TEE images interpretation is performed prior to the initiation of the study.

Transesphageal Echocardiography

Resuscitative TEE is performed in the emergency department by an emergency physician who had been trained in emergency ultrasound and advanced training in basic TEE examination. The TEE is performed with a Mindray M9 ultrasound machine via a multiplane probe (Mindray DC70, Shenzhen, China).

Introduction of TEE probe is assisted with administration of intravenous fentanyl or midazolam, when necessary for sedation. Application of lignocaine spray to the posterior pharynx is performed for the non-intubated patients.

To specifically evaluate the aorta with suspected BTAI, we recommend using our department protocol-driven focused TEE exam. The exam is started by advancing the probe 30-40cm in a transverse plane (0-20°) to develop the mid-esophageal 4 chamber view (ME 4C). After centering the image on the left ventricle, and rotating the omniplane to 130° the mid-esophageal long axis (ME LAX) view is obtained, providing the first view of the ascending aorta. The aortic root can be visualized in this view and the proximal ascending aorta can be further

examined by withdrawing the TEE probe. After centering the image, the ascending aorta can be evaluated in both planes with the mid-esophageal ascending aorta short and long axis view (ME Asc Ao SAX and ME Asc Ao LAX) at 0° and 90° omniplane respectively.

Following this, the focused was brought back to ME 4 chamber view, rotates the probe counterclockwise to the left and posteriorly from the perspective of the head, until the descending aorta comes to view. After reducing the image depth to magnify the image of the aorta, the descending thoracic aorta (DTA) is then visualized entirely by advancing the probe 5-6 cm. By withdrawing the probe slowly, the aortic arch appears in a longitudinal view in the mid-esophageal DTA SAX view. The steps above are then repeated at 90° omniplane to obtain the ME DTA LAX view in the longitudinal plane. Finally, the aortic arch is evaluated throughout its visible length at the proximal part of the descending aorta using multiplane scanning. TEE images will be recorded.

CT Angiography

CT angiography is performed using 64 slices dual detector CT machine (Toshiba Aquilion CX 2010, Japan). Findings of the CT scan is examined by a radiologist with more than 10 years experienced who is blinded to the TEE findings done beforehand.

Data Collection & Image Analysis

Injuries are assigned one of 4 grades of BTAI: grade 1 (intimal tear), grade II (intramural hematoma), grade III (pseudoaneurysm) and grade IV (rupture).

The interpretation of TEE and CTA will be entered into the data collection form. The findings of the TEE by the emergency physicians will be compared with CTA images which are reported by the radiologist.

3.2 Study Population

All trauma patients with suspected BTAI in the emergency department (ED)

3.3 Inclusion Criteria

All trauma patients with suspected BTAI in the emergency department (ED).
Suspected BTAI are defined by the presence of at least one of the following criteria
1. high risk mechanism of injury (deceleration or crush injury),
2. clinical findings (external chest trauma or unexplained hypotension) or
3. chest Xray findings suspicious of BTAI (mediastinal widening, a blurred aortic knob, apical capping of the lung, a depressed left bronchus, a displaced nasogastric, mediastinal widening, or fractured first or second ribs).

3.4 Exclusion Criteria

1. Children (age under 18 years) will not be eligible for inclusion in this study.
2. Patients with contraindication to TEE such as suspected esophageal injury or pathology

4.0 Withdrawal Criteria

Subjects can choose to withdraw at any time. Subjects may be withdrawn if the investigator deems that it is detrimental or risky for the subject to continue. Withdrawn subjects will not be replaced.

5.0 Study Duration and Timeline

The study is expected to go on from **15-03-2022 until 15-3-2023** for 1 year. The data will be collected at the point of time during patient's attendance at the emergency department. There will not be any follow up.

6.0 Sample Size

We calculate the sample size to determine whether resuscitative TEE is accurate to diagnose BTAI compare to CT scan as a gold standard.

The null hypothesis is set as AUC 0.5 (meaning no discriminating power), Type 1 error of 0.05 and power of 80%. Based on previous data (17), with a precision of 10%, and an expected proportion of BTAI on CTA of 10%, the sample size required was 45.

Taking into account the potential for 20% incomplete data, we included 56 patients for the final analysis. AUROC sample size calculation was performed using an online statistic calculator. (**https://www.scistat.com/samplesize/samplesize.php**)

7.0 Statistical Analysis Plan

Descriptive statistics will be applied to patient characteristics and diagnostic findings of the resuscitative TEE and CTA.

The diagnostic performance of the TEE will be expressed as sensitivity (Se) and specificity (Sp), with their [confidence intervals at 95%]. Areas under receiver operating characteristic (ROC) curves will be compared for the correlation between ROC areas obtained from the two test modalities.

Inter-rater reliability will be calculated with the Cohen's kappa test. Chance agreement is reflected by a kappa of 0, whereas a kappa of 1.0 constitutes perfect agreement.
A p value < 0.05 is considered to indicate a statistically significant difference.

Statistical analysis will be performed using the Statistical Package for the Social Sciences, version 20.0 (IBM, USA).

8.0 Risk and benefit to study participants

Participation to the present study does not involve additional risk for the patient. The complications associated with TEE (bleeding, esophageal injury) and CTA (contrast allergy, worsening kidney function) are rare. Both investigations are part of the routine work up for chest trauma patients and the benefits outweigh the risks involved.

The findings of the study will contribute to the evidence of the role of TEE in diagnosing BTAI for chest trauma patients in ED.

9.0 Ethical Consideration

The study will be conducted in accordance with the principles of Good Clinical Practice (ICH Harmonized Tripartite Guidelines for Good Clinical Practice 1996 Directive 91/507/EEC;D.M. 15.7.1997), the Helsinki declaration and the international rules governing clinician experimentations worldwide. The participants, by signing this protocol, declare that they will fully conform to the described procedures and instructions.
Approval has been obtained from the National Institutes of Health and the Medical Research and Ethics Committee, Ministry of Health Malaysia.

10.0 Informed Consent

Those patients meeting inclusion and exclusion criteria at the emergency department after the diagnosis of blunt throracic aortic injury (BTAI) is suspected, will be provided with information about the study.

Specifically, research investigator will then explain to patient (or next of kin, if deemed necessary) that the patient will receive the usual diagnostic workup for BTAI. Written informed consent form will be provided together with the verbal explanation.

The patient or next of kin will be allowed sufficient time to consider their participation in the study. If the patient or next of kin object to the inclusion of the patient in the study, their views will be respected.

11.0 Privacy and Confidentiality

All the information obtained in this study will be kept and handled in a confidential manner. No identifiers of the subjects will be captured by the data collection form. Subjects will be fully anonymized and a subject ID number will be assigned to each data collection form. Individuals involved in this study, qualified monitors, auditors and governmental or regulatory authorities may inspect the study data, where appropriate and necessary. The data captured via the data collection form will be entered into a computer that is password protected and analyzed using the aforementioned software installed in the computer.

On completion of study, data in the computer will be copied to CDs. Data in the computer will be erased. The informed consent forms, data collection forms and CDs will be stored under locked cabinets by the investigators and maintained for 3 years after the final publication and presentation. After 3 years, the data will be destroyed. The subjects may request for the results from the investigators at the end of the final write up if they are interested.

12.0 Conflict of Interest

The investigators declare they have no conflict of interest.

13.0 Publication Policy

The trial results will be published in an established peer-reviewed journal. No personal information of the subjects will be revealed during the publication process. Relevant permissions will be obtained prior to publication.

14.0 Termination of Study

The sponsor may decide to terminate the study at any time. Subjects will be informed if the study is terminated and follow-up visits will be arranged if needed.

References

1. Teixeira PG, Inaba K, Barmparas G, Georgiou C, Toms C, Noguchi TT, Rogers C, Sathyavagiswaran L, Demetriades D. Blunt thoracic aortic injuries: an autopsy study. J Trauma. 2011 Jan;70(1):197-202. doi: 10.1097/TA.0b013e3181df68b3. PMID: 21217494.

2. Mouawad, N.J., Paulisin, J., Hofmeister, S. et al. Blunt thoracic aortic injury – concepts and management. J Cardiothorac Surg 15, 62 (2020). https://doi.org/10.1186/s13019-020-01101-6

3. Osman A, Fong CP, Wahab SFA, Panebianco N, Teran F. Transesophageal Echocardiography at the Golden Hour: Identification of Blunt Traumatic Aortic Injuries in the Emergency Department. J Emerg Med. 2020 Sep;59(3):418-423. doi: 10.1016/j.jemermed.2020.05.003. Epub 2020 Jun 23. PMID: 32591302.

4- O'Conor, C. (2004). Diagnosing traumatic rupture of the thoracic aorta in the emergency department. Emergency medicine journal : EMJ. 21. 414-9. 10.1136/emj.2002.001834.

5. Rubin, Geoffrey & Leipsic, Jonathon & Schoepf, Uwe & Fleischmann, Dominik & Napel, Sandy. (2014). CT Angiography after 20 Years: A Transformation in Cardiovascular Disease Characterization Continues to Advance. Radiology. 271. 633-52. 10.1148/radiol.14132232.

6. Hahn LD, Prabhakar AM, Zucker EJ. Cross-sectional imaging of thoracic traumatic aortic injury. Vasa. 2019 Jan;48(1):6-16. doi: 10.1024/0301-1526/a000741. Epub 2018 Sep 28. PMID: 30264668

7. Goarin JP, Cluzel P, Gosgnach M, Lamine K, Coriat P, Riou B. Evaluation of transesophageal echocardiography for diagnosis of traumatic aortic injury. Anesthesiology. 2000 Dec;93(6):1373-7. doi: 10.1097/00000542-200012000-00005. PMID: 11149428.

8. Vignon, Philippe & Boncoeur-Martel, Marie & François, Bruno & Rambaud, Geoffray & Maubon, Antoine & Gastinne, Hervé. (2001). Comparison of Multiplane Transesophageal Echocardiography and Contrast-enhanced Helical CT in the Diagnosis of Blunt Traumatic Cardiovascular Injuries. Anesthesiology. 94(4): 615-22. doi: 10.1097/00000542-200104000-00015.

9. Shiga T, Wajima Z, Apfel CC, Inoue T, Ohe Y. Diagnostic accuracy of transesophageal echocardiography, helical computed tomography, and magnetic resonance imaging for suspected thoracic aortic dissection: systematic review and meta-analysis. Arch Intern Med. 2006;166(13):1350-1356. doi:10.1001/archinte.166.13.1350

10. Leichtle SW, Singleton A, Singh M, Griffee MJ, Tobin JM. Transesophageal echocardiography in the evaluation of the trauma patient: A trauma resuscitation transesophageal echocardiography exam. J Crit Care. 2017. doi:10.1016/j.jcrc.2017.04.007

11- Shyu, Jeffrey & Khurana, Bharti & Soto, Jorge & Biffl, Walter & Camacho, Marc & Diercks, Deborah & Glanc, Phyllis & Kalva, Sanjeeva & Khosa, Faisal & Meyer, Benjamin & Ptak, Thomas & Raja, Ali & Salim, Ali & West, O. & Lockhart, Mark. (2020). ACR Appropriateness Criteria® Major Blunt Trauma. Journal of the American College of Radiology. 17. S160-S174. 10.1016/j.jacr.2020.01.024.

12- Chirillo F, Totis O, Cavarzerani A, Bruni A, Farnia A, Sarpellon M, Ius P, Valfrè C, Stritoni P. Usefulness of transthoracic and transoesophageal echocardiography in recognition and management of cardiovascular injuries after blunt chest trauma. Heart. 1996 Mar;75(3):301-6. doi: 10.1136/hrt.75.3.301. PMID: 8800997; PMCID: PMC484291.

13- Chatzikonstantinou, Anastasios & Krissak, Radko & Flüchter, Stephan & Artemis, Dimitrios & Schaefer, A & Schönberg, Stefan & Hennerici, Michael & Fink, Christian. (2012). CT Angiography of the Aorta Is Superior to Transesophageal Echocardiography for Determining Stroke Subtypes in Patients with Cryptogenic Ischemic Stroke. Cerebrovascular diseases (Basel, Switzerland). 33. 322-8. 10.1159/000335828.

14. Mirvis SE, Shanmuganathan K, Buell J, Rodriguez A. Use of spiral computed tomography for the assessment of blunt trauma patients with potential aortic injury. J

Trauma. 1998 Nov;45(5):922-30. doi: 10.1097/00005373-199811000-00014. PMID: 9820704.

15. Bruckner BA, DiBardino DJ, Cumbie TC, Trinh C, Blackmon SH, Fisher RG, Mattox KL, Wall MJ. Critical evaluation of chest computed tomography scans for blunt descending thoracic aortic injury. Ann Thorac Surg. 2006 Apr;81(4):1339-46. doi: 10.1016/j.athoracsur.2005.11.012. PMID: 16564268.

16.Cinnella G. Use of CT scan and transesophageal echocardiography in blunt thoracic trauma. Intensive Care Med. 1998 Sep;24(9):986-7. doi: 10.1007/s001340050702. PMID: 9917204

17. Smith MD, Cassidy JM, Souther S, Morris EJ, Sapin PM, Johnson SB, Kearney PA. Transesophageal echocardiography in the diagnosis of traumatic rupture of the aorta. N Engl J Med. 1995 Feb 9;332(6):356-62. doi: 10.1056/NEJM199502093320603.