Research Protocol

Point-of-Care Ultrasound Screening for Thoracic Aortic Aneurysm in Hypertensive Patients in the Emergency Department

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Introduction

Thoracic aortic aneurysm (TAA) is the dilatation of aortic wall by definition and is usually asymptomatic.(1) The annual incidence of TAA is 5 to 10 per 100,000 people.(2) TAA could evolve into aortic dissection (AD) which is a lethal disorder with an hourly mortality rate of 1-2% from symptom onset if untreated.(3) In 2020, approximately 1,950 admissions fell under the diagnosis group of aortic aneurysm and dissection in Hong Kong, with about 350 deaths recorded among these patients.(4) And in a local study of TAA in a hypertensive clinic, a prevalence of 7.5% was found in a study sample of 1,529 participants using pocket-size mobile echocardiographic devices.(5)

To screen TAA patients, point-of-care ultrasound (POCUS) is a quick and specific imaging tool that is easily accessible in the ED. POCUS demonstrated a pooled sensitivity of 89% (95% CI: 82-94%) and a specificity of 92% (95% CI: 88-95%) for the direct sign of type A aortic dissection from various studies.(6) In the context of emergency department (ED), we often deal with catastrophic acute AD; however, we aim to screen TAA patients in the ED before they rupture. Early detection of TAA in high-risk group could reduce the need of emergency operations, allowing elective aortic interventions. Surgical intervention is often indicated when aortic diameter ≥ 5.5cm.(7) There is a causal relationship between the blood pressure and ascending thoracic aortic diameter.(8) As a result, targeted screening in the hypertensive population might prevent TAA from progressing to a ruptured state, thereby reducing mortality and morbidity.

In a local study, more than 30% of type A aortic dissection (TAAD) patients were misdiagnosed in the ED. Among these misdiagnosed patients, many presented with normal blood pressure and relatively mild signs and symptoms, resulting in their triage in lower categories.(9) Additionally, the absence of a POCUS ultrasound exam was identified as an

independent factor associated with misdiagnosis in the ED.(9) Therefore, performing a POCUS scan could help identify TAA and TAAD patients in the ED even when they have a low pretest probability.

Aim

This study aims to evaluate the prevalence of TAA in hypertensive patients identified in the ED using POCUS.

Objectives

1. To investigate the number of hypertensive patients presenting to the ED with aortic diameter ≥ 4.5 cm as indicated by POCUS
2. To evaluate the number of patients with confirmed TAA as verified by CTA
3. To evaluate the agreement of aortic diameter measurement between CTA and POCUS

Hypotheses

1. POCUS can identify TAA by measuring the aortic diameter.

Methodology

This prospective cohort study is coordinated by the Accident and Emergency Medicine Academic Unit of the Chinese University of Hong Kong (CUHK) in collaboration with the Department of Surgery and the Department of Medicine and Therapeutics of CUHK. The investigators will carry out this study in the accident and emergency department at Prince of Wales Hospital (PWH). PWH serves a population of 1.6 million people in the New Territories of Hong Kong and is the main teaching hospital of CUHK. The investigators will be trained for POCUS before the commencement of the study and the images will be audited by an echocardiologist.

<u>Inclusion and exclusion criteria for participants</u>

Inclusion criteria:

1. Adult patients aged ≥ 18 years attending the ED during the study period
2. Known history of hypertension or newly diagnosed hypertension in the ED

Exclusion criteria:

1. Known history of aortic aneurysm or dissection
2. Previous thoracic aortic interventions or endovascular stenting
3. Patients in cardiopulmonary resuscitation

4. Traumatic patients
5. Patients refuse to participate the study

Sample size calculation

According to previous studies, the estimated prevalence of TAA in hypertensive patients in a clinic was 7.5% and the area under the curve for POCUS detecting aortic dilation was 0.857.(5, 10) With a confidence level of 95% and margin of error of 5%, 1186 patients will be needed.(11)

To ensure that this study has enough participants after accounting for a 20% inadequate visualization of the POCUS image, the investigators will need to recruit 1483 participants. The investigators target to complete the recruitment within 12 months.

Data collection

The investigators trained with POCUS will recruit and screen patients in the ED during the study period using an ultrasound device throughout the study and all images will be stored for regular review by an echocardiologist.

POCUS screening will be conducted to measure the maximum diameters at end diastole of the aortic root, ascending aorta, aortic arch, and descending thoracic aorta. The internal diameter will be measured perpendicular to the axis of blood flow and leading edge to leading edge in accordance with the guidelines set forth by the American College of Cardiology.(12) Measurements of the aortic root and ascending aorta will be taken using parasternal long-axis views, while the aortic arch will be assessed from the suprasternal view. The descending thoracic aorta will be examined using modified apical 2-chamber and subcostal views. The investigators will also specifically look for an intimal flap, pericardial effusion and aortic regurgitation.

The investigators will inform the emergency physicians under the following conditions:

1. patient has an aortic diameter ≥ 5cm
2. patient has an intimal flap, pericardial effusion or moderate aortic regurgitation

If physicians identify a clinical possibility of TAA, these patients will be referred to cardiothoracic surgeons. If there is a suspicion of acute aortic syndrome, the ED physicians will consult cardiothoracic surgeon urgently ± CTA in the ED as usual practice.

Relevant clinical data (such as past medical history, laboratory results, operation records etc.) will also be collected. In addition, the investigators will follow up with the patients for 28 days to monitor mortality and any advanced imaging performed outside the ED.

Outcome measurement

The primary outcome is the number of patients with TAA (a maximum aortic diameter of ≥ 4.5 cm and/or ≥ 50% localized enlarged diameter relative to the adjacent normal segment as indicated by POCUS).

The secondary outcomes include the number of patients with confirmed TAA as verified by CTA, BMI for all participants, the number of CTA scans conducted for TAA confirmation, the number of surgical interventions performed among TAA patients, the ICU admission rate, ICU length of stay, hospital length of stay and mortality, proportion of adequate visualisation of POCUS studies obtained, agreement of aortic diameter measurement between CTA and POCUS, and signs and symptoms of TAA patients presenting to the ED. In addition, the investigators will assess the 28-day all-cause mortality and any advanced imaging done outside the ED for evaluating the aorta.

Statistical analysis

Patients with a maximum aortic diameter ≥ 4.5 cm and/or ≥ 50% localized enlarged diameter relative to the adjacent normal segment are regarded as TAA while those with an aortic diameter < 4.5 cm are regarded as non-TAA. Comparison of baseline characteristics and aortic size measurements will be made between these two groups of patients. Categorical variables will be compared with Chi square test or Fisher's exact test. Continuous variables will be compared using Student's t-test or Mann-Whitney U test, based on the results of the Shapiro-Wilk W test. Binary logistic regression analysis will be used to identify the risk factors that associated with TAA independently and to predict the presence of TAA. Variables with a $p < 0.2$ from the univariate analysis will be included in the stepwise logistic regression model. In patients who underwent a CTA, the investigators will assess the agreement of aortic diameter measurements between CTA and POCUS using Bland-Altman analysis. All statistical analyses and visualisations will be done using R or Prism GraphPad.(13, 14) A significance level of 0.05 will be considered statistically significant.

Patients with missing data on certain variables will be removed from that particular analysis. POCUS studies with inadequate visualisation of all views will be discarded.

Ethics

All participants will provide written informed consent. Patients' relatives can provide consent if the patient is not mentally capable of doing so. If no relatives are present in the ED, the investigators will obtain deferred consent as soon as the patient is awake. If the patient passes away before they can consent to this study, all images and data collected will be discarded. No images and data will be used without consent. Participants are allowed to withdraw from the study at any time during the study period and their data will be discarded. This study will be conducted in full compliance with the Declaration of Helsinki and the principles of Good Clinical Practice. The investigators will seek ethical approval from our local review committee.

Funding and Sponsor

There is no funding or sponsorship for this study.

Potential Conflicts of Interest

The PI and CI have declared no potential conflicts of interest.

Safety Management

Ultrasound is a safe screening tool and does not cause any adverse effects to patients. Any incidental findings of aortic abnormalities will be reported to the attending physician. The investigators will abort the POCUS scan immediately and inform the attending physician in the event of any deterioration. Necessary resuscitation will be initiated without further delay.

Cost and Benefit for Participants

There is no additional charge or reward for participation in this study.

Confidentiality and privacy

Ultrasound images will be stored in both the device and the CUHK internal drive. All clinical data will be collected using the CU WebForm and will be kept confidential. Data will be destroyed 7 years after the publication of the study. Signed consent forms will be saved in a locked cabinet in the research office.

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