A RANDOMIZED CONTROLLED TRIAL OF THE EFFECTIVENESS OF "CHEST PAIN EVALUATION AT EMERGENCY ROOM" (CHEER) PROTOCOL IN THE ED OF HUSM: A MODEL FOR MALAYSIAN EMERGENCY DEPARTMENTS

MOHAMMAD FIRDAUS BIN BOLONG @ MOHD DARWIS

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE (EMERGENCY MEDICINE)

UNIVERSITI SAINS MALAYSIA

2020

ACKNOWLEDGEMENT

First and foremost, praise to Allah SWT and peace and blessings to His Prophet Muhammad SAW for the completion of this trial.

I would like to thank my Primary Supervisor, Dr Andey Rahman for his help in this trial and its writing. I'd also want to thank the Head of Emergency Department of Hospital USM, AP Dr Tuan Hairulnizam for his continuing support in the trial.

Not forgetting the Division of Research and Innovation for RUI Grant given to the study during the duration of trial.

Next is thanks to other co-researchers in this study Prof Dato' Dr Nik Hisamuddin, Dr Zikri Ahmad, Dr Abu Yazid Muhammad, all from the Emergency Department of Hospital USM and also Dr Wan Yus Haniff Wan Isa from Internal Medicine Department of Hospital USM for their input in creating, conducting and also writing of this thesis. I'd also want to thank Research Assistant Amirah in helping with the paperworks of the study. Further thanks to colleagues and also all staffs of Hospital USM involved in this study.

Finally I'd like to thank my parents, my wife Nurull Huda Abdul Majid, my children Nurull Humaira and Nurull Huwaidah for their understanding and sacrifice during my post graduate years.

TABLE OF CONTENTS

ABSTRAK

Latar Belakang

Rawatan bagi pesakit dewasa yang mengalami sakit dada berisiko rendah adalah salah satu masalah di Jabatan Kecemasan di Malaysia. Cara-cara seperti penggunaan nisbah Creatin-Kinase/Creatin-Kinase MB digunakan dalam merawat pesakit yang mengalami sakit dada risiko rendah di Malaysia. Kadang-kadang pesakit dimasukkan ke wad perubatan untuk observasi kerana wujudnya perbezaan dalam perawatan sakit dada berisiko rendah dan ini akan menyebabkan keramaian pesakit di Jabatan Kecemasan, atau wujudnya rujukan yang tidak perlu dan kemasukan ke dalam wad perubatan yang tidak perlu, seterusnya memburukkan lagi waktu menunggu untuk dimasukkan ke dalam wad.

Metodologi

Kajian terkawal rawak prospektif ini memasukkan 53 pesakit yang mempunyai sakit dada risiko rendah yang datang ke Jabatan Kecemasan Hospital USM. Pesakit dirawakkan ke bahagian rawatan biasa mengikut tatacara penanganan sakit dada di HUSM atau ke bahagian rawatan CHEER yang menggunakan ECG bersiri dan ujian Troponin I bersiri. Butiran pesakit seperti umur, sifat sakit dada, dermografi, bacaan ECG, skor TIMI dan HEART dikira sewaktu rawatan. Pesakit akan di susul selepas 6 minggu dan 6 bulan dalam menentukan prevalensi kejadian serangan jantung besar, kemasukan semula ke jabatan kecemasan untuk sakit dada, dan jangka waktu pesakit di Hospital dan juga kadar discaj awal dari Jabatan Kecemasan.

Keputusan

Kajian menunjukkan protocol CHEER mempunyai kadar jangka waktu lebih singkat rawatan di Jabatan Kecemasan dan juga kadar discaj lebih awal di Jabatan Kecemasan berbanding rawatan biasa. Protokol CHEER dan rawatan biasa mempunyai tiada perbezaan dalam Kejadian Serangan Jantung Besar dan Kemasukan Semula ke Jabatan Kecemasan untuk sakit dada.

Kesimpulan

Protokol CHEER memendekkan jangka waktu rawatan hospital dan menggalakkan kadar discaj awal manakala tidak mepunyai perbezaan dalam hasil melibatkan Serangan Jantung Besar dan kemasukan semula ke Jabatan kecemasan untuk sakit dada.

Kata Kunci

Sakit Dada, Jabatan Kecemasan, skor HEART

ABSTRACT

Background

Management of low risk chest pain in adults is a problem in emergency department in Malaysia. Traditional use of CK/CKMB ratio among others has been used to manage patients presenting with low risk chest pain in Malaysia. Sometimes patients are admitted to the medical ward for observation due to the ambiguity of management of low risk chest pain thus creating overcrowding in ED or unnecessary referral and admission to the medical wards, which will occupy beds and worsen backlog of admission

Methods

This prospective randomised control trial included 53 patients with low risk chest pain admitted to Emergency department in Hospital USM. Patients were randomised to either a standard care arm for chest pain treatment according to current HUSM guideline or CHEER (Chest Pain Evaluation in Emergency Room) protocol arm which involves 8 hours observation with serial ECG and Troponin test. Patients information such as age, chest pain characteristics, demography, ECG findings, HEART and TIMI score were calculated during the stay. Patients were followed up after 6 weeks and 6 months to determine prevalence of Major Adverse Cardiac Event, Readmission to ED for chest pain, and their length of stay in hospital and rate of early discharge from ED.

Results

Study shows that CHEER protocol has overall shorter length of stay at ED or hospital and has higher early discharge rate compared to standard care. There is

however no difference between CHEER protocol and standard care in terms of incidence of Major Adverse Cardiac Event and readmission to ED due to chest pain.

Conclusion

CHEER protocol shortens length of stay and promotes early discharge but there was no difference in outcome of patients regarding Major Adverse Cardiac Event and readmission due to chest pain.

Keyword

Chest Pain, Emergency Department, HEART score

CHAPTER 1: INTRODUCTION

1.1 Overview of Cardiovascular Disease Burden in Malaysia

According to Malaysian Cardiac Care Performance in 2016, Malaysia's performance of 2012 is below average for estimated mortality from cardiovascular disease.[1] This fact correlates with Malaysia's performance in percentage of daily smoker in 2012. This points toward the fact that cardiovascular disease is the leading cause of mortality in Malaysia as well as worldwide.[2]

NCVDACS 2014-2015 registry stated that 17,771 patients were admitted for Acute Coronary Syndrome. Of all the patients admitted for ACS, more than half (53.9%) were for Non- ST elevation MI and Unstable Angina.[3]

Risks of Cardiovascular disease are obesity, smoking, hypertension, diabetes mellitus and also hyperlipidemia.[4] According to National Health and Morbidity Survey 2019, it is reported that 3.4 million adult in Malaysia has at least 2 major risk factors of cardiovascular disease and 1.7 million adult has 3 major risk factors namely hypertension, diabetes and hyperlipidemia.[5]

It is reported by WHO in 2011 that Malaysia government spent 7% of total government budget on healthcare, even though relatively Malaysians spent less than peers in developing countries on healthcare, mainly due to government subsidies.[6] National Health and Morbidity Survey 2019 also reports that there is an increasing trend of expenditure from total monthly income towards healthcare from 2015 (4.6%) to 2019 (5.1%). And it is worth noting that 11% of patients had to borrow from family members or friends for health expenditures.[5]

Due to the burden of financial implications and also mortality and morbidity, Malaysian Health Ministry has been actively educating the public in reducing the risk factors of coronary arterial disease, as well as coming out with Primary and Secondary prevention of Cardiovascular Disease CPG 2017 for primary healthcare givers. [4]

1.2 Problems in Managing Patients with Chest Pain in Emergency Department

One of the local data available was a census in Hospital Kuala Lumpur during 2014 where 466 patients were admitted to the emergency department with initial impression of Acute Coronary Syndrome but after evaluation 339 (73%) were discharged.[7]

Risk stratification is now very important to reduce overcrowding in Emergency Department (ED), as well as to reduce needless referral and admission to cardiac wards. Not all patients presenting with chest pain of cardiac origin needed to be admitted. ADAPT trial mentioned that risk stratification is important so that patients who are at low risk of developing ACS can be discharged with follow up.[8]

In Emergency Department Hospital USM (HUSM), patients presented with chest pain are attended to and underwent several tests namely serial Electrocardiogram (ECG), Creatine-Kinase to Creatine-Kinase MB (CK/CKMB) ratio, before decision for referral to medical department for admission.

Bloods are sent to the lab and waiting times can be long, especially during peak hours, as well as risk of needless admissions that will occupy beds in the medical wards, in turn will deprive off bed from patients who really needs hospital beds.[9]

In view of this, multiple clinical scoring, chest pain unit protocols and also accelerated diagnostic protocols are produced and applied to risk stratify patients presenting with chest pain.[10]

1.3 Justification of Study

The Emergency Physicians must distinguish between those who require urgent management of a serious problem such as acute coronary syndrome (ACS) and those with more benign entities who do not require admission.

There is a significant number of patients with chest pain who falls under the category of low probability ACS. Traditionally, these patients would either be admitted to medical ward for observation and further workup or would be discharged directly from the ED after investigations.

Inadvertent discharge of patients with acute coronary syndrome from the emergency department is associated with increased mortality and liability, whereas inappropriate admission of patients without serious disease is neither indicated nor cost-effective.

There is a need for a protocol or a pathway regarding low risk chest pain to reduce the congestion in emergency department. A few studies has been done regarding this problem over the years.[9,11,12]

But there is an emerging trend in the developed countries using HEART pathway trial to risk stratify patients according to risk to get major adverse cardiac events (MACE), and those who are low risk are discharged home with outpatients appointment for reassessment and cardiac testing, which can reduce emergency department overcrowding.[11]

1.4 Chest Pain Evaluation in Emergency Room Protocol (CHEER)

Our Emergency Department intends to set up (Chest Pain Evaluation in Emergency Room) **CHEER protocol** which aims to provide a good medical care and judicious use of investigations at a lower cost for patients presenting to ED with chest pain but with low probability for acute coronary syndrome, but not sufficiently low to be allowed home.

Chest Pain Evaluation in Emergency Room (CHEER) Protocol is developed by HUSM Emergency Department together with Cardiology Unit HUSM after discussions with National University of Singapore to prepare a guideline for patients presenting to ED with low probability for ACS. CHEER protocol are based on the HEART pathway randomised trial and are fine-tuned to get the best of outcomes for patients as well as reducing the burden of unnecessary admission into the medical wards.[13]

The objective of this study is to differentiate patients who need to be admitted for further workout from those who can be discharged safely without risking any Major Cardiac Event. It is also aimed to reduce unnecessary admissions to medical ward which will reduce overcrowding in Emergency Department and also medical ward.

CHAPTER 2: INTRODUCTION AND LITERATURE REVIEW

2.1 INTRODUCTION

According to Malaysian Cardiac Care Performance in 2016, Malaysia's performance of 2012 is below average for estimated mortality from cardiovascular disease.[1] This fact correlates with Malaysia's performance in percentage of daily smoker in 2012. This points toward the fact that cardiovascular disease is the leading cause of mortality in Malaysia as well as worldwide.[2]

NCVDACS 2014-2015 registry stated that 17,771 patients were admitted for Acute Coronary Syndrome. Of all the patients admitted for ACS, more than half (53.9%) were for Non- ST elevation MI and Unstable Angina.[3]

Risks of Cardiovascular disease are obesity, smoking, hypertension, diabetes mellitus and also hyperlipidemia.[4] According to National Health and Morbidity Survey 2019, it is reported that 3.4 million adult in Malaysia has at least 2 major risk factors of cardiovascular disease and 1.7 million adult has 3 major risk factors namely hypertension, diabetes and hyperlipidemia.[5]

It is reported by WHO in 2011 that Malaysia government spent 7% of total government budget on healthcare, even though relatively Malaysians spent less than peers in developing countries on healthcare, mainly due to government subsidies.[6] National Health and Morbidity Survey 2019 also reports that there is an increasing trend of expenditure from total monthly income towards healthcare from 2015 (4.6%) to 2019 (5.1%). And it is worth noting that 11% of patients had to borrow from family members or friends for health expenditures.[5]

Due to the burden of financial implications and also mortality and morbidity, Malaysian Health Ministry has been actively educating the public in reducing the risk factors of coronary arterial disease, as well as coming out with Primary and Secondary prevention of Cardiovascular Disease CPG 2017 for primary healthcare givers. [4]

One of the local data available was a census in Hospital Kuala Lumpur during 2014 where 466 patients were admitted to the emergency department with initial impression of Acute Coronary Syndrome but after evaluation 339 (73%) were discharged.[7]

Risk stratification is now very important to reduce overcrowding in Emergency Department (ED), as well as to reduce needless referral and admission to cardiac wards. Not all patients presenting with chest pain of cardiac origin needed to be admitted. ADAPT trial mentioned that risk stratification is important so that patients who are at low risk of developing ACS can be discharged with follow up.[8]

In Emergency Department Hospital USM (HUSM), patients presented with chest pain are attended to and underwent several tests namely serial Electrocardiogram (ECG), Creatine-Kinase to Creatine-Kinase MB (CK/CKMB) ratio, before decision for referral to medical department for admission.

Bloods are sent to the lab and waiting times can be long, especially during peak hours, as well as risk of needless admissions that will occupy beds in the medical wards, in turn will deprive off bed from patients who really needs hospital beds.[9]

In view of this, multiple clinical scoring, chest pain unit protocols and also accelerated diagnostic protocols are produced and applied to risk stratify patients presenting with chest pain.[10]

Chest Pain Evaluation in Emergency Room (CHEER) Protocol is developed by HUSM Emergency Department with help of Cardiology Unit HUSM after discussions with National University of Singapore to act as a guideline for patients presenting to ED with low probability for ACS. CHEER protocol are based on the HEART Pathway randomised trial and are fine tuned to get the best of outcomes for patients as well as reducing the burden of needless admission into the medical wards.[13]

2.2 LITERATURE REVIEW

1. CHEST PAIN VISITS AND VARIATIONS OF CADIAC TESTING

There is a lot of variation in investigating chest pain in the world. It is documented in 2000 that chest pain is the second most common cause of ED visits in the USA, just second to abdominal complaints, and this accounts for billions of dollars in annual hospital costs.[14]. NCVDACS 2014-2015 registry stated that 17,771 patients were admitted for Acute Coronary Syndrome. Of all the patients admitted for ACS, more than half (53.9%) were for Non- ST elevation MI and Unstable Angina.[3] There is however a small percentage of patients who doesn't need admission and actually is at low risk of developing Major Adverse Cardiac Events.

There is no local data and protocol in managing chest pain visits which are not clear cut Acute Myocardial Infarction in Malaysia. The management and protocol usually

vary between different centres. USM for example are using CK/CKMB ratio to investigate for cardiac muscle necrosis or injury.

It was mentioned by Amsterdam et al in 2010 that in managing low risk chest pain patients, a lot of methods have been developed to strike the balance in managing patients with low risk chest pain in the USA, namely Chest Pain Units, Accelerated Diagnostic Protocols and clinical scores.[10] In managing all these chest pain visits to ED Safavi et al found out there's variations in different emergency departments in assessing and managing chest pain complaints in the US, in which different cares are given by different hospitals.[14]

2. CHEST PAIN UNITS

Chest pain units, first developed in the United States, attempt to improve diagnostic accuracy, shorten length of stay, and save money. Such units take patients who have been assessed to be at low or moderate risk and are protocol driven. Typically, patients are closely monitored for 6-12 hours, subjected to a battery of biochemical tests, serial ECGs and often ST segment monitoring and an exercise ECH. IF all these tests are negative the patients are sent home, but if positive or equivocal the patient is admitted for further investigation and treatment.[15]

A scientific statement from the American Heart Association 2010 recommended that chest pain units with accelerated diagnostic protocol with a confirmatory test to exclude ischemia are safe, accurate, and cost effective in low-risk patients presenting with chest pain.[10]

In archives of Cardiovascular Diseases (2009) Eric Durand et al reported that Chest Pain Unit in France can exclude an ACS safely. Of the 906 patients studied, 27.9% had an ACS. Non-ischaemic cardiac etiologies and non-cardiac etiologies were found in 12.6% and 7.0% patients, respectively. A final diagnosis of chest pain of undetermined origin was made in 51.5% of patients; among these, 6.5% patients were re-admitted to the CPU. Thirty day follow-up revealed that only one patient had subsequent confirmation of coronary arterial disease requiring further hospitalisation.[16]

A study at Townsville hospital by Roberts L et al reported that the Chest Pain Admission Unit (CPAU) resulted in a reduction in the percentage of 'missed' cases of ACS, an increased rate of apparently appropriate angiograms and a relative decrease in proportion of admitted patients diagnosed with ACS compared with those with unspecified chest pain.[17]

Zeynep Cakir et al reported that fast and effective evaluation of ischemic chest pain in the ED and correct management of patients by correct determination of the risk factors provides a high level of cost-effectiveness. Every ED should determine an algorithm for patients admitted with chest pain and physicians should obey this algorithm.[18]

It was reported by Elad Asher et al in PLOS ONE, 2015 that fast and definitive investigation of patients with acute chest pain according to pre-specified protocol provides better quality of care with shortened hospitalisation length, might even

reduce health care expenses. This approach can also contribute towards lowering the workload and burden in the internal medicine department.[19]

Rydman et al found that patients are more satisfied with rapid diagnosis in the Chest Pain assessment unit than with inpatient stays with acute chest pain.[20] This was supported by Richards et al where it is found that Chest Pain assessment units are acceptable from patients perspective.[21]

From outcomes point of view, Cullen MW et al found that a chest pain assessment unit does not increase long-term adverse outcomes in patients with chest pain at intermediate risk for an acute event.[22]

3. SCORING IN PREDICTING MAJOR ADVERSE CARDIAC EVENTS

There are a lot of scoring in the literature regarding predicting probability of major cardiac events. 3 major predicting scores are mainly used, namely HEART, TIMI and GRACE scores. Different scores having different parameters and cut off points in determining which patients are predicted to develop Major Adverse Cardiac Events. In 2016, Poldevaart et al did a research on comparisons between GRACE, TIMI and HEART scores and their outcomes on predicting MACE. It is found out that HEART score outperforms both TIMI and GRACE in predicting major adverse cardiac events, thus recommending the use of HEART score in working up chest pain in the emergency department.[23]

4. ACCELERATED DIAGNOSTIC PROTOCOL FOR CHEST PAIN IN EMERGENCY DEPARTMENT

There are a few accelerated diagnostic protocols for chest pain in emergency room done over the years. One of it is ADAPT trial by Than et al using TIMI score and serial Troponin at 0 and 2 hours.[9]

Another one is the HEART Pathway Randomised Trial by Mahler et al by using HEART score and serial troponin.[11]

In 2016, Stopyra et al compared the 2 diagnostic protocols, and concluded that both protocols are sensitive for Major Adverse Cardiac Event, but HEART outperformed ADAPT in identifying the patients who are at low risk for discharge.[8]

5. HEART SCORE

HEART scoring was developed in 2008 by Backus et al to risk-stratify patients presenting with chest pain to emergency department but without ST changes in the ECG. It is used to quickly and reliably predict the outcome of patients with chest pain presented to emergency department, thus determining the aggressiveness of approach and management of the patient.[24]

It consists of 5 components, mnemonic of the HEART itself.

H stands for history taken from the patients. Nature of chest pain is described by the patient, alongside with localisations, relations to stress and exercise, radiation of pain, use of sublingual GTN and concomitant symptoms. Non-suspicious history is given score of 0, moderately suspicious history is given score of 1, and maximum of 2 score given to highly suspicious history.

E stands for ECG. If the ECG is normal as per Minnesota criteria, score 0 is given. If there is changes in the ECG; non specific changes such as bundle branch block, LVH strain pattern, digoxin related changes, then score of 1 is given. Maximum score of 2 given to patients with ECG of ST segment changes.

A stands for Age. IF the patients age is less than 45, score of 0 is given. If the age is between 45 to 65 years old, score 1 is given. Maximum score of 2 given to patients with age 65 years old and above.

R stands for risk factor. Risk factors of the patients presented with chest pain is counted. Risk factors involved are hypertension, currently treated diabetes, current or recent smoker (less than 1 month), hypercholestremia, family history of coronary arterial disease, and obesity. If none risk factors are present, score 0 is given. If any 1 or 2 risk factors present, score 1 is given. Maximum score of 2 given to patients with 3 or more risk factors. 2 points also given to patients with previous history of coronary revascularisation, stroke, peripheral arterial disease and myocardial infarction

T stands for Troponin levels taken from the patients. Troponin taken will be Troponin I. Score of 0 is given to patients with troponin level less than threshold level of positivity. Score 1 is given if troponin I level is less between once and twice level of positivity. Score 2 is given for troponin level more than twice level of positivity.

End points of the HEART study are Coronary Arterial Bypass Graft (CABG), Percutaneous Coronary Intervention (PCI), acute myocardial infarction (AMI) and death.

The study formulated that patients with combined HEART score of 0-3 warrants for early discharge as this group of patients only have risk of 2.5% in reaching endpoints. HEART score of 4-6 warrants admission and must be treated for ACS awaiting non-invasive investigations as this group of patients has 20.3% risk of developing adverse outcome. Patients with HEART score 7 or above warrants aggressive treatment and invasive strategies without preceding non-invasive investigations as they hold the risk of 72.7% reaching end point.[24]

6. HEART PATHWAY RANDOMISED TRIAL

In 2015, Simon Mahler et al found out that when compared to routine standard care, HEART pathway reduced objective cardiac testing within 30 days, increases early discharge and also shortens length of stay in the hospital. [11]

A further paper on 1-year outcome on the HEART PATHWAY RANDOMISED TRIAL also suggested that the study has 100% non-predictive value of 1 year safety outcomes without increasing downstream hospitalisations and Emergency department revisits.[25]

In the HEART pathway, patients Troponin I level was taken twice, on presentation and also after 3 hours.

CHAPTER 3: METHODOLOGY

3.1 RESEARCH QUESTION

CHEER protocol at ED HUSM is better than the traditional management which are still being practised by Emergency departments across Malaysia.

The factors concerned would be less major adverse cardiac events at 6 weeks, less length of stay at ED, higher rate of early discharge from ED and lower rate of readmission to ED for chest pain of ischemic region.

- Comparison between the two groups regarding major cardiac events at 6 weeks
- What is the length of stay in the Emergency Department and Hospital?
- What is the rate of early discharge from ED between the two groups?
- What is the rate of readmission to ED for chest pain of ischemic origin?

RESEARCH OBJECTIVES

General:

- To evaluate the effectiveness of CHEER protocol on the low cardiac risk patients presenting to ED HUSM.

Specific primary:

- To compare the prevalence of major adverse cardiac events (MACE) within 6 weeks among low cardiac risk patients with and without cheer protocol in ED HUSM.

Specific secondary:

- To compare the length of stay at ED or hospital among the low cardiac risk patients with and without cheer protocol in ED HUSM
- To compare the early discharge among the low cardiac risk patients with and without cheer protocol in ED HUSM
- To compare the readmission to ED for chest pain of ischemic origin among the low cardiac risk patients with and without cheer protocol in ED HUSM

3.2 METHODOLOGY

Study design

A randomized control trial to confirm the benefit of CHEER Protocol at ED, HUSM

Patients of low probability Acute Coronary Syndrome according to initial HEART score were included in the study.

Patient selection by randomization was performed.

One arm was in the CHEER Protocol group which used our own accelerated diagnostic protocol.

The other was in usual standard care group. All the investigations and management were according to present standard care of HUSM.

The performance of CHEER Protocol in comparison to standard routine care was then determined.

Target Group

All patients with chest pain of probable cardiac ischemia origin excluding those diagnosed with Acute Coronary Syndrome.

Source Populations

Chest pain patients with low probability Acute Coronary Syndrome after screening with inclusion and exclusion criteria presented to ED HUSM

Sampling Frame

16 months

Location of Study

Observation ward and CHEER unit, Emergency Department, Hospital USM

Sampling Method

Inclusion criteria

- All patients with chest pain of probable cardiac ischemia origin presented ED, HUSM
- Initial normal or non-diagnostic ECG
- Normal initial cardiac biomarkers (if done)
- Initial HEART score 3 or less

Exclusion criteria

- Patients diagnosed as definite Acute Coronary Syndrome such as Unstable Angina, Non-ST Elevation MI, and ST Elevation MI
- ECG with ST shift (ST depression or ST Elevation) or with dynamic changes in serial ECG
- Hemodynamically unstable

- Patients with other significant illness such as heart failure, Pneumonia etc.

Major adverse cardiac events (MACE)

It would include the following:

- Acute Myocardial Infarction
- Positive catheterization or PCI
- CABG
- All-cause mortality

Procedure

Intervention Group: CHEER Protocol

One group was managed according to CHEER Protocol which utilized our own accelerated diagnostic protocol.

They were clinically observed and investigated according to our **CHEER Protocol**

Clinical observation and evaluation will be carried for at least 8 hours.

In particular, 3 sets of ECGs and 2 testing of Troponin I were done during this clinical observation period.

Troponin I was taken on presentation and 3 hours after presentation.

ECG were done at 0 hours, 3 hours and 5 hours.

And then HEART score was calculated to categorize low, medium and high-risk group.

Medium and high-risk group were admitted to hospital and treatment were given accordingly.

Low risk group patients were allowed home.

According to HEART score, those with HEART score of 3 and below belongs to the Low Risk Group.

Initially, we intended to offer these low risk group patients an **Exercise Stress Test** at ED before going home since ETT appointment at HUSM can be from 3 months to 6 months.

If negative, patient was to be allowed home.

ETT is one of the function cardiac stress test employed in addition to low risk ACS assessment (CHEER Protocol in our case) in many Emergency Department of more developed countries.

This depended on approval of acquiring cardiac stress test.

Control Group: Standard Care

In standard care, patients were managed according to standard approach to chest pain in HUSM. Serial ECG were done and CK/CKMB ratio were taken and calculated. Positive CK/CKMB ratio taken is 6% and more.

Doctors in charge observed the patient and decided to admit or discharge the patient home according to his/her clinical judgement without standard time of observation.

FOLLOW UP

Follow up were conducted by telephone interview at 6 weeks and 6 months.

OUTCOME

We looked into the followings of low cardiac risk patients with and without CHEER Protocol in ED HUSM over a period of 6 weeks and 6 months.

1. Incidence of Major Adverse Cardiac Events within 6 weeks

2. Number of patients being readmitted to ED for chest pain of ischaemic origin

3. Early discharge rate from Emergency Department

4. Length of stay in ED or Hospital

OPERATIONAL DEFINITION AND OUTCOME

Low Risk Chest Pain is defined by cumulative HEART score less than 3.

MACE is Major Adverse Cardiac Event, defined by ST Elevation Myocardial Infarction, Non-STEMI with cardiogenic shock, Cardiac arrest or Cardiac Failure, and all-cause mortality.

Readmission for Chest Pain is defined by revisit or second visit to ED due to chest pain within 6 weeks or 6 months telephone follow up.

Early Discharge is defined by discharge from emergency department only

Length of Stay (**LOS**) in Emergency Department or Hospital is defined by time of patient registered to Emergency Department until the time patient decided for discharge from Emergency Department or ward.

Acute Coronary Syndrome comprises of ST Elevation Myocardial Infarction, Non-ST Elevation Myocardial Infarction, and Unstable Angina

Alere Triage Troponin I Test

Alere Triage Troponin I Test is a fluorescence immunoassay to be used with the Alere Triage Meters for quantitative determination of Troponin I in EDTA

anticoagulated whole blood and plasma specimens. The test is to be used as an aid in the diagnosis of acute coronary syndrome.

The test procedure involves the addition of several drops of an EDTA anticoagulated whole blood or plasma specimen to the sample port on the Test Device. After addition of the specimen, the whole blood cells are separated from the plasma using a filter contained in the Test Device. The specimen reacts with fluorescent antibody conjugates and flows through the Test Device by capillary action. Complexes of each fluorescent antibody conjugate are captured on discrete zones specific for each analyte.

The Test Device is inserted into the Alere Triage Meter (hereafter referred to as Meter). The Meter is programmed to perform the analysis after the specimen has reacted with the reagents within the Test Device. The analysis is based on the amount of fluorescence the Meter detects within a measurement zone on the Test Device. The concentration of the analyte(s) in the specimen is directly proportional to the fluorescence detected. The results are displayed on the Meter screen in approximately 20 minutes from the addition of specimen. All results are stored in the Meter memory to display or print when needed. Ii connected, the Meter can transmit results to the lab or hospital information system

SAMPLE SIZE CALCULATION

1. Major Adverse Cardiac Events (MACE)

2 proportions:

Standard = 11.3% (JP Stopyra et. al, The HEART Pathway Randomized Controlled Trial One-year Outcomes, 2018)

CHEER pathway = 0.1%

Significance level (α) = 0.05

Power ($1-\beta$) = 0.9

P_0 = proportion of those who developed MACE = 0.11

P_1 = estimated proportion of development of MACE = 0.01

Calculated sample size (n) = 116

Addition of 20% expected drop out = 23

Sample size per group = 116 + 23 = 139

Total sample size = 278

2. Length of stay

2 means

Standard 2.6 days (SD 1.07) (Elad Asher et al PLOS ONE 2015 Jan 26)

$\alpha = 0.05$

$1- \beta = 0.9$

$\sigma = 1.07$

δ= estimated difference of mean length of stay between 2 groups = 1.6

N = 10

Addition of 20% expected drop out = 2

Sample size per group = 10 + 2 =12

Total Sample size = 24

3. Early Discharge

2 proportion

Standard 18.4% (Simon A Mahler et al, The HEART Pathway Randomize trial,

CHEER Pathway 50% ahajournal.org, 2015)

$\alpha = 0.05$

$1- \beta = 0.9$

P0 = Proportion of those who were able to be discharged = 0.184

P1 = Estimated proportion of those who were able to be discharged = 0.5

N = 45

Addition of 20% expected drop out = 9

Sample size per group = 54

Total sample size = 108

4. ED readmission for chest pain

2 proportions:

Standard = 12% (JM Poldervaart et. al, Effect of Using the HEART Score in Patients with Chest Pain in the Emergency Department, 2017)

CHEER pathway = 0.2%

Significance level (α) = 0.05

Power ($1-\beta$) = 0.9

P_0 = proportion of those who represent with chest pain = 0.12

P_1 = estimated proportion of those who represent chest pain with CHEER pathway = 0.02

Calculated sample size (n) = 135

Addition of 20% expected drop out = 27

Sample size per group = 135 + 27 = 162

Total sample size = 324

Data Collection

Data were collected from the patient using data collection form in the Appendices page. It was collected by the attending doctors after patient's inclusion and exclusion criteria are met and patient consented to be in the study. Randomisation were done by the investigators after case is reported to the researchers. Anamnesis and patients' history, ECG and vital signs available from the patient's folder were also taken after consent is given. Each patient was numbered randomly to maintain confidentiality of the study and identifications will only be known by the researchers.

Data collection were done once patients consented and all criteria were met. Phone interviews were done after 6 weeks and 6 months as well as tracing patient's record to collect the data and outcome.

Statistical Analysis

- Descriptive Analysis determined the patient's demography such as age, gender and also ethnicity.
- Simple logistic regression was conducted to determine the association between Major Adverse Cardiac Events (MACE), early discharge,

readmission to ED for chest pain of ischemic origin among the low cardiac risk patients with type of treatment group

- Simple linear regression was conducted to determine the association between length of stay at ED or hospital among the low cardiac risk patients with type of treatment group
- After that, multivariate analysis was done for all the dichotomous outcome namely incidence of Major Adverse Cardiac Event, Readmission due to chest pain, and also early discharge.

Dummy Tables

Comparison of patient characteristics between CHEER and control group

Variables	**CHEER (n=)**	**Control (n=)**	χ^2	***Df***	**p-value**
	n (%)	**n (%)**			
Age group (Year)					
Below 45 years old					
45-64 years old					
Sex					
Male					
Female					
Ethnicity					
Malay					
Non-Malay					

CHEER protocol randomized control trial patient characteristics

Characteristics	**CHEER**		**Control**	
	Frequency (f), n=	Percentage (%)	Frequency (f)	Percentage (%), n=
Age (Years) mean, SD				