SENARAI SEMAKAN UNTUK BUKU LAPORAN AKHIR GERAN USM JANGKA PENDEK

NAMA PENYELIDIK UTAMA	:	**NIK HISAMUDDIN BIN NIK AB RAHMAN**
NAMA CO-RESEARCHER	:	
TAJUK GERAN	:	CLINICAL EVALUATION OF 1-STEP QUALITATIVE HEART-SPECIFIC FATTY ACID BINDING PROTEIN (H-FABP) TEST (CardioDetect®) AND QUANTITATIVE CARDIAC TROPONIN T, FOR THE DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION IN THE EMERGENCY DEPARTMENT.
NO.AKAUN	:	

SENARAI SEMAKAN SEMASA PENYERAHAN BUKU LAPORAN AKHIR
(Sila Tandakan (√) Pada Kotak Yang Berkenaan)

NO.	PERKARA	ADA	TIADA
1.	Borang Laporan Akhir Projek Penyelidikan USM Jangka Pendek	/	
2.	Borang Laporan Hasil Penyelidikan, PPSP	/	
3.	i) Salinan Menuskrip	/	
	ii) Salinan surat/email bukti penghantaran kepada mana-mana journal	/	
4.	Penyata Perbelanjaan (Financial Statement) (Sila dapatkan daripada Jabatan Bendahari)	/	
5.	Laporan Komprehensif (termasuk kertas persidangan atau seminar dan penerbitan saintifik hasil daripada projek ini)	/	
6.	Surat pemakluman penghantaran Laporan Akhir ke Bhg. Penyelidikan	/	

Nota:

* Sila buat 3 salinan buku laporan Akhir
* No. 1-5 - Perlu dimasukkan dalam Buku Laporan Akhir
* No.6 - Hantar terus Kepada Cik Amra Othman (RCMO) hanya salinan sahaja kepada Bhg. R&D, PPSP

UNIVERSITI SAINS MALAYSIA

LAPORAN AKHIR PROJEK PENYELIDIKAN JANGKA *PENDEK*

FINAL REPORT OF SHORT TERM RESEARCH PROJECT

Sila kemukakan laporan akhir ini melalui Jawatankuasa Penyelidikan di Pusat Pengajian dan Dekan/Pengarah/Ketua Jabatan kepada Pejabat Pelantar Penyelidikan

1. Nama Ketua Penyelidik: PROF MADYA DR NIK HISAMUDDIN NIK AB RAHMAN
Name of Research Leader

☑ Profesor Madya/ *Assoc. Prof.* ☐ Dr./ *Dr.* ☐ Encik/Puan/Cik *Mr/Mrs/Ms*

2. Pusat Tanggungjawab (PTJ): JABATAN PERUBATAN KECEMASAN PUSAT PENGAJIAN SAINS PERUBATAN
School/Department

3. Nama Penyelidik Bersama:
Name of Co-Researcher

4. Tajuk Projek: CLINICAL EVALUATION OF 1-STEP QUALITATIVE HEART-SPECIFIC FATTY ACID BINDING PROTEIN (H-FABP) TEST (CardioDetect®) AND QUANTITATIVE CARDIAC TROPONIN T, FOR THE DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION IN THE EMERGENCY DEPARTMENT.

5. Ringkasan Penilaian/*Summary of Assessment*:	Tidak Mencukupi *Inadequate*		Boleh Diterima *Acceptable*	Sangat Baik *Very Good*	
	1	2	3	4	5
i) Pencapaian objektif projek: *Achievement of project objectives*	☐	☐	☐	☐	☑
ii) Kualiti output: *Quality of outputs*	☐	☐	☐	☑	☐
iii) Kualiti impak: *Quality of impacts*	☐	☐	☐	☑	☐
iv) Pemindahan teknologi/potensi pengkomersialan: *Technology transfer/commercialization potential*	☐	☐	☑	☐	☐
v) Kualiti dan usahasama : *Quality and intensity of collaboration*	☐	☐	☐	☐	☑
vi) Penilaian kepentingan secara keseluruhan: *Overall assessment of benefits*					

6. **Abstrak Penyelidikan**
(Perlu disediakan di antara 100 - 200 perkataan di dalam **Bahasa Malaysia dan juga Bahasa Inggeris**. Abstrak ini akan dimuatkan dalam Laporan Tahunan Bahagian Penyelidikan & Inovasi sebagai satu cara untuk menyampaikan dapatan projek tuan/puan kepada pihak Universiti & masyarakat luar).
Abstract of Research
(An abstract of between 100 and 200 words must be prepared in Bahasa Malaysia and in English).
This abstract will be included in the Annual Report of the Research and Innovation Section at a later date as a means of presenting the project findings of the researcher/s to the University and the community at large)

AS ATTACHED

7. **Sila sediakan laporan teknikal lengkap yang menerangkan keseluruhan projek ini.**
[Sila gunakan kertas berasingan]
Applicant are required to prepare a Comprehensive Technical Report explaning the project.
(This report must be appended separately)

AS ATTACHED

Senaraikan kata kunci yang mencerminkan penyelidikan anda:
List the key words that reflects your research:

Bahasa Malaysia	*Bahasa Inggeris*
SERANGAN JANTUNG	MYOCARDIAL INFARCTION
LEMAK SPESIFIK JANTUNG	HEART SPECIFIC FATTY ACID
ENZIM KARDIAK	CARDIAC ENZYME

8. **Output dan Faedah Projek**
Output and Benefits of Project

(a) * **Penerbitan Jurnal**
Publication of Journals
(Sila nyatakan jenis, tajuk, pengarang/editor, tahun terbitan dan di mana telah diterbit/diserahkan)
(State type, title, author/editor, publication year and where it has been published/submitted)

CLINICAL EVALUATION OF 1-STEP QUALITATIVE HEART-SPECIFIC FATTY ACID BINDING PROTEIN (H-FABP) TEST (CardioDetect®) AND QUANTITATIVE CARDIAC TROPONIN T, FOR THE DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION IN THE EMERGENCY DEPARTMENT.

PUBLISHED IN THE A RESEARCH BOOK FORM ISBN 978-83838782-6 BY LAMBERT ACADEMIC PUBLISHING

(b) **Faedah-faedah lain seperti perkembangan produk, pengkomersialan produk/pendaftaran paten atau impak kepada dasar dan masyarakat.**
State other benefits such as product development, product commercialisation/patent registration or impact on source and society.

tiada

* Sila berikan salinan/*Kindly provide copies*

(c) **Latihan Sumber Manusia**
Training in Human Resources

i) Pelajar Sarjana:
Graduates Students
(Perincikan nama, ijazah dan status)
(Provide names, degrees and status)

DR AHMAD SUHAILAN (PELAJAR MMED GRADUATED 2009)

ii) Lain-lain:
Others

9. **Peralatan yang Telah Dibeli:**
Equipment that has been purchased

Tandatangan Penyelidik
Signature of Researcher

5/12/10

Tarikh
Date

Komen Jawatankuasa Penyelidikan Pusat Pengajian/Pusat
~~Comments by the Research Committees of Schools/Centres~~

This quantum research project has been completed successfully and objectives achieved.

The output of the project included a named (Swapping web) dissertation (Student by Ahmad Suhailan) graduated in 2009 and a publication in the UAP (Student Abstract Publication)

This report has been assessed by an independent assessor and approved by the PTJ PPD committee

2/2/2011
Tarikh
Date

TANDATANGAN PENGERUSI
JAWATANKUASA PENYELIDIKAN
PUSAT PENGAJIAN/PUSAT
Signature of Chairman
[Research Committee of School/Centre]

BORANG LAPORAN HASIL PENYELIDIKAN
PPSP

Tajuk geran: **CLINICAL EVALUATION OF 1-STEP QUALITATIVE HEART-SPECIFIC FATTY ACID BINDING PROTEIN (H-FABP) TEST (CardioDetect®) AND QUANTITATIVE CARDIAC TROPONIN T, FOR THE DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION IN THE EMERGENCY DEPARTMENT.**

Penyelidik:**Nik Hisamuddin Nik Ab Rahman**
Jenis geran: **Jangka Pendek**
Tempoh geran:**2 Tahun**

Jenis laporan: Laporan Kemajuan [ ] Alatan di beli [ ] Ya:nyatakan.....

Laporan Akhir*: [/] [ ] Tidak

OBJEKTIF SPESIFIK KAJIAN (sama spt dalam proposal asal)	**SECARA RINGKAS TERANGKAN PENCAPAIAN/HASIL**	**OBJEKTIF TERCAPAI ATAU TIDAK**
To compare the diagnostic indices [sensitivity, specificity, positive predictive value, negative predictive value, receiver operating characteristic (ROC) curve] of the qualitative CardioDetect® assay and the quantitative cardiac troponin T test, in diagnosing AMI in the ED, according to the time of onset of chest pain.	The CardioDetect® was more sensitive and had a higher NPV than TnT during the first 12 hours of onset of chest pain.	Yes
To verify whether there was any improvement in the diagnostic indices (sensitivity, specificity, positive predictive value, negative predictive value, ROC) of CardioDetect® test in diagnosing AMI when repeated 1 hour after an initial negative result, in patients with acute ischemic type chest pain presenting to the ED.	This study also concluded that repeating the CardioDetect® test 1 hour after an initial negative result improved the sensitivity, specificity, PPV and NPV of the test especially during the first 4 hours after the onset of chest pain.	Yes
To determine whether there was any improvement in the diagnostic indices (sensitivity, specificity, positive predictive value, negative predictive value, ROC curve) of CardioDetect® assay in diagnosing AMI when used in combination with cardiac troponin T test in patient with acute ischemic chest pain presenting to the ED.	It was shown that the combination test of CardioDetect® and TnT had a better diagnostic accuracy than individual test especially during the first 4 hours after AMI.	Yes

- *Laporan Akhir perlu disertakan salinan manuskrip dan surat yang dihantar kepada mana-mana jurnal untuk penerbitan.*

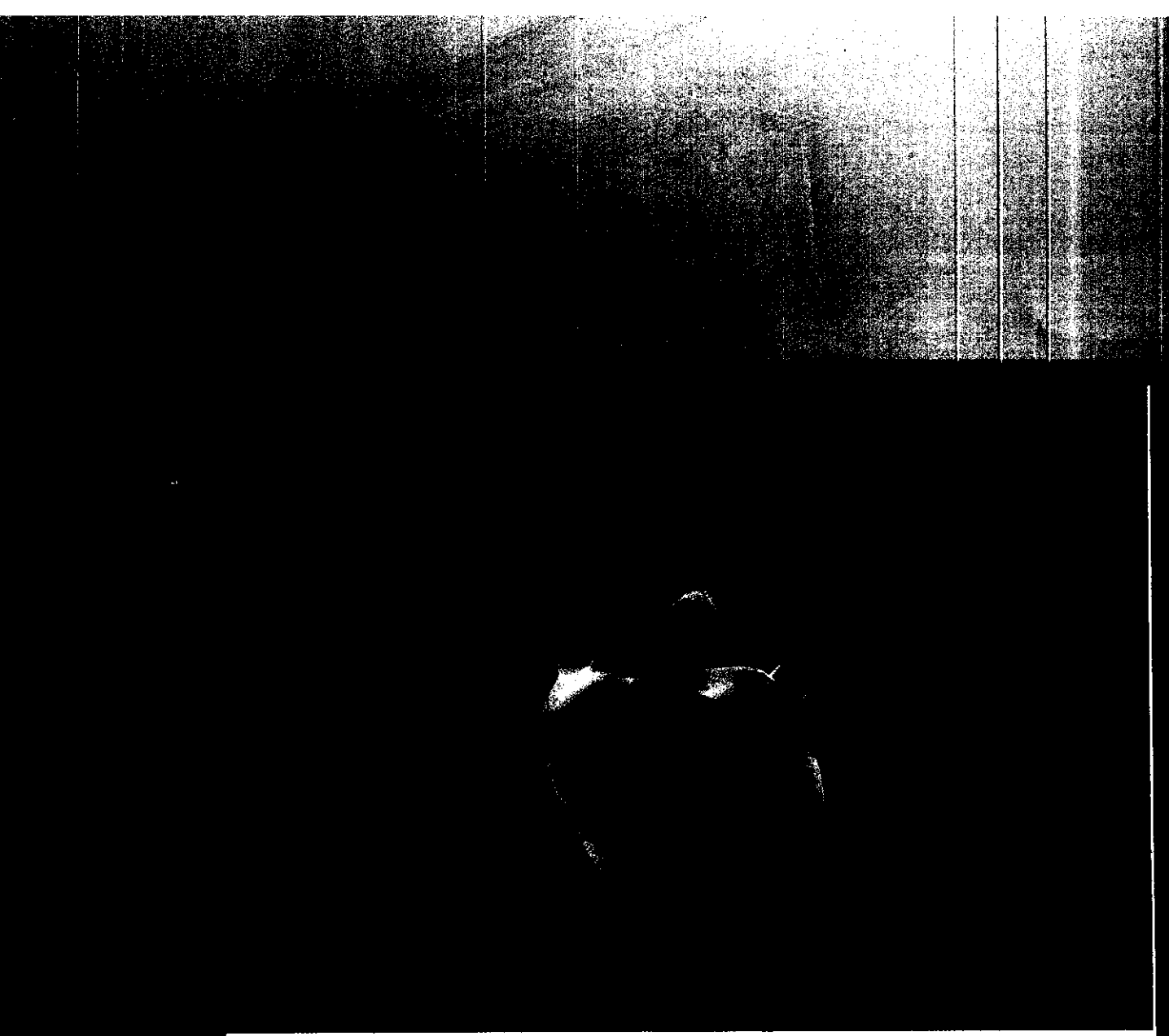
Nama Penyelidik Utama (PI):**PROF MADYA DR NIK HISAMUDDIN BIN NIK AB RAHMAN**
Tarikh: 5HB Didember 2010

TT:

UNIVERSITI SAINS MALAYSIA
JABATAN BENDAHARI
KUMPULAN WANG PENYELIDIKAN GERAN USM(304)
PENYATA PERBELANJAAN SEHINGGA 30 NOV 2010

Jumlah Geran:	RM	33,860.00	Ketua Projek:	Nik Hisamuddin Nik Ab. Rahman, Dr
Peruntukan 2008 (Tahun 1)	RM	19,110.00	Tajuk Projek:	Clinical Evaluation of 1-Step Qualitative Heart-Specific Fatty Acid Binding Protein (H-FABP) Test (CardioDetect) and Quantitative Cardiac Troponin T, for The Diagnosis of Acute Myocardial Infarction in The Emergency Department
Peruntukan 2009 (Tahun 2)	RM	14,750.00		
			Tempoh:	1 Jun 2008 - 31 Mei 2010
			No.Akaun:	304/PPSP/6131607

Kwg	Akaun	PTJ	Projek	Donor	Peruntukan Projek	Perbelanjaan Tkumpul Hingga Tahun Lalu	Peruntukan Semasa	Tanggungan Semasa	Bayaran Tahun Semasa	Belanja Tahun Semasa	Baki Projek
304	11000	PPSP	6131607		-	-	-	-	-	-	-
304	14000	PPSP	6131607		5,460.00	-	5,460.00	-	-	-	5,460.00
304	15000	PPSP	6131607		-	-	-	-	-	-	-
304	21000	PPSP	6131607		-	4,465.50	(4,465.50)	-	678.00	678.00	(5,143.50)
304	22000	PPSP	6131607		-	-	-	-		-	-
304	23000	PPSP	6131607		400.00	-	400.00	-		-	400.00
304	24000	PPSP	6131607		-	-	-	-		-	-
304	25000	PPSP	6131607		-	-	-	-		-	-
304	26000	PPSP	6131607		-	-	-	-		-	-
304	27000	PPSP	6131607		27,500.00	8,526.00	18,974.00	-		-	18,974.00
304	28000	PPSP	6131607		-	-	-	-		-	-
304	29000	PPSP	6131607		500.00	11,939.00	(11,439.00)	-	2,678.83	2,678.83	(14,117.83)
304	32000	PPSP	6131607		-	-	-	-	-	-	-
304	35000	PPSP	6131607		-	-	-	-	-	-	-
304	A11559	PPSP	6131607		-	-	-	5,000.00	-	5,000.00	(5,000.00)
					33,860.00	24,930.50	8,929.50	5,000.00	3,356.83	8,356.83	572.67



Nik Hisamuddin Nik Ab Rahman
Ahmad Suhailan

QUALITATIVE HEART-SPECIFIC FATTY ACID BINDING PROTEIN (H-FABP) TEST

CLINICAL EVALUATION IN MYOCARDIAL INFARCTION

LAP LAMBERT Academic Publishing

Early and correct diagnosis of patients admitted to the hospital with symptoms suggestive of acute myocardial infarction (AMI) is paramount to ensure appropriate therapy is given to minimize myocardial injury and improve clinical outcome. The urgency in recognizing and treating patients with an AMI as early as possible has been repeatedly stressed and reiterated in various guidelines that lead to the well-known phrase of 'Time loss is myocardium loss'. As a consequence, the patient's prognosis will deteriorate.In situation like these, cardiac biomarkers may be invaluable in establishing a diagnosis of AMI in the ED setting. A number of established cardiac biomarkers have been available in the market and several new promising assays with better sensitivity have been discovered. A recent potential cardiac biomarker that shows release kinetics similar to myoglobin is heart-type fatty acid-binding protein (H-FABP). We believe that this diagnostic kit that detects H-FABP at the bedside, still needs further evaluation especially to assess its performance and practicality to detect AMI in patients presenting with chest pain in the ED setting.

Nik Hisamuddin Nik Ab Rahman, Ahmad Suhailan
Associate Professor Dr Nik Hisamuddin Nik Ab Rahman, MBChB, MMed, ACEP. Obtained his basic medical degree from the University of Glasgow. Current position include the head and consultant Emergency Medicine in the University Sains Malaysia. Main interests include trauma and injury prevention, resuscitation and acute pain management.

9 783838 387826 **978-3-8383-8782-6**

FINAL TECHNICAL REPORT

Coronary heart disease and myocardial infarction is one of the predominant causes of mortality and morbidity in Malaysia (Ministry of Health statistics 2004). Cardiovascular disease has been the fourth most common cause of hospitalization in this country since 2001. From 2001-2006, heart disease (together with the disease of the pulmonary circulation) has persistently been the second principal cause of death in government hospitals (Malaysian Ministry of Health Medical Statistics, 2001-2006). In 2002, cardiovascular disease accounted for 118,262 admissions into Ministry of Health hospitals (7.2% of total admissions), but killed 8384 of them, accounting for 24.5% of all deaths in government hospitals (Chua, 2005). Thus, heart disease is an important cause of premature deaths in Malaysia, resulting in significant social and economic implications to the nation.

Early and correct diagnosis of patients admitted to the hospital with symptoms suggestive of acute myocardial infarction (AMI) is paramount to ensure appropriate therapy is given to minimize myocardial injury and improve clinical outcome (De Luca *et al.*, 2004). The urgency in recognizing and treating patients with an AMI as early as possible has been repeatedly stressed and reiterated in various guidelines that lead to the well-known phrase of 'Time loss is myocardium loss'. With the passing of time and further delay in diagnosing AMI and administration of reperfusion therapy, more cardiac muscle will be damaged (Hasche *et al.*, 1995). As a consequence, the patient's prognosis will deteriorate. To expedite diagnosis, the AHA/ACC Guidelines for the management of patients with ST-elevation myocardial infarction (STEMI) in 2004 recommended that an

electrocardiogram (ECG) should be performed and interpreted by an experienced physician within 10 minutes of arrival to emergency department (ED). If reperfusion therapy is deemed indicated, the decision whether to use fibrinolytic therapy or percutaneous coronary intervention (PCI) should be made within the next 10 minutes (Antman *et al.*, 2004). Therefore, diagnosing an AMI as early and as accurate as possible is the most critical phase in the treatment of patient presenting with chest pain to the ED. Once a definitive diagnosis can be made, prompt steps can be taken to limit the myocardial necrosis including instituting reperfusion therapy.

In situation like these, cardiac biomarkers may be invaluable in establishing a diagnosis of AMI in the ED setting. A number of established cardiac biomarkers have been available in the market and several new promising assays with better sensitivity have been discovered. Recently a one-step immunochromatographic point-of-care test called CardioDetect® has been developed for H-FABP. It is a qualitative assay that detects H-FABP in patient's whole blood sample and results are available within 15 minutes. It allows diagnosis of AMI within 30 minutes of chest pain (Chan *et al.*, 2003). Due to its rapid onset of positivity, the CardioDetect® has the potential to detect and exclude AMI in patients presenting early to the ED with chest pain. Patients without ST-elevation on the initial ECG and without positive troponin but with suspected acute ischemic chest pain are the most difficult to handle in terms of diagnosis. With the rapid detection of H-FABP, CardioDetect® has the potential to exclude non-ST-elevation MI in this group of patients who presents early after onset of chest pain to the ED. Many studies have been conducted on H-FABP, but few have investigated the diagnostic accuracy and practicality

of CardioDetect. We believe that this diagnostic kit that detects H-FABP at the bedside, still needs further evaluation especially to assess its performance and practicality to detect AMI in patients presenting with chest pain in the ED setting.

GENERAL OBJECTIVES

To evaluate the diagnostic indices and clinical utility of qualitative CardioDetect test kit in diagnosis of AMI in the emergency department, in comparison to quantitative cardiac troponin T assay.

1.1. SPECIFIC OBJECTIVES

1. To compare the diagnostic indices [sensitivity, specificity, positive predictive value, negative predictive value, receiver operating characteristic (ROC) curve] of the qualitative CardioDetect assay and the quantitative cardiac troponin T test, in diagnosing AMI in the ED, according to the time of onset of chest pain.

2. To verify whether there was any improvement in the diagnostic indices (sensitivity, specificity, positive predictive value, negative predictive value, ROC curve) of CardioDetect test in diagnosing AMI when repeated 1 hour after an initial negative result, in patients with acute ischemic type chest pain presenting to the ED.

3. To determine whether there was any improvement in the diagnostic indices (sensitivity, specificity, positive predictive value, negative predictive value, ROC curve) of CardioDetect assay in diagnosing AMI when used in combination with cardiac troponin T test in patient with acute ischemic chest pain presenting to the ED.

4. To assess inter-observer variability in interpreting results of qualitative CardioDetect test in the ED.

This study was a prospective cross-sectional study. It was conducted from Feb 2008 until September 2008 and the source population were all patients who presented with chest pain suggestive of AMI to ED at HUSM, Kubang Kerian, Kelantan during the stipulated study period. HUSM is a regional tertiary centre with an attendance rate exceeding 45,000 patients per year. HUSM is also a teaching institution dedicated to undergraduate and postgraduate training including Emergency Medicine. This study was undertaken as a dissertation study under the Department of Emergency Medicine HUSM and Universiti Sains Malaysia short term-grant. Ethical approval was obtained from the department board review and hospital ethics committee on the 13th February 2008 [reference USMKK/PPP/JEPeM 199.3(10)].

1.2. Selection of subjects

The reference population were all adult patients presenting to general hospital Accident and Emergency in Kota Bharu district. The source population were all adult patients who presented with chest pain suggestive of AMI to the ED at HUSM. The eligible population was the source population fulfilling the inclusion and exclusion criteria.

1.2.1. Inclusion criteria

1. Adult patients 18 years old or above.
2. All patients presenting to the ED with ischemic chest pain that is less than 36 hours duration of onset..

1.2.2. Exclusion criteria

1. Patients with a history of recent muscle injury (<3 days), including intramuscular injection.
2. Patients with acute or chronic skeletal muscle damage or disorders including rhabdomyolysis, dermatomyositis, muscular dystrophy and polymyositis
3. Patients with renal insufficiency as defined by serum creatinine > 200μmol/L.

4. Critically ill patients, including cardiogenic shock, septic, intubated and ventilated patients
5. Patients who has had a recent myocardial infarction or received fibrinolytic therapy or angioplasty, within the last 14 days prior to presentation to the ED.

1.3. Sampling method and sampling size

Sampling method for this study was obtained through universal sampling. Patients were enrolled during all shifts and days of the week. The sample size was calculated by a HUSM biomedical statistician with reference to 'Statistical Evaluation of medical tests for classification and prediction; Study Design and hypothesis testing' (Margeret Sullivan Pepe Oxford University Press 2003). The variables used in the calculation were as follows:

Type I error is 5% ($\alpha = 0.05$)

Power of study = 0.8

87 patients required which included 20% dropout rate in this study.

SAMPLING SIZE

$$n_{(diseased)} = \frac{[\, z^{1-\alpha} \sqrt{TPF_0(1-TPF_0)} + z^{1-\beta} \sqrt{TPF_1(1-TPF_1)}\,]^2}{(TPF_1 - TPF_0)^2} = \mathbf{48}$$

$$n_{(non\ diseased)} = \frac{[\, z^{1-\alpha} \sqrt{FPF_0(1-FPF_0)} + z^{1-\beta} \sqrt{FPF_1(1-FPF_1)}\,]^2}{(FPF_1 - FPF_0)^2} = \mathbf{24}$$

$z^{1-\alpha} = 1.96$ $z^{1-\beta} = 0.84$ Power = 80%
Type I error 5%

$TPF_1 = 0.40$ $TPF_0 = 0.60$
$FPF_1 = 0.30$ $FPF_0 = 0.10$

Sample size = 48 + 24 + (adjusted to 20% dropout rate) = **87**

Data entry and analysis were performed with Statistical Packages for Social Sciences (SPSS Version 11.0 for windows, Chicago, United States of America). Mean and standard deviation were obtained for all the numerical variables (Age and serum Creatinine). Descriptive statistics (frequencies) were obtained for most categorical variables.

Sensitivity, specificity, PPV and NPV were obtained for the CardioDetect and TnT (individually and in combination) and for the repeated CardioDetect test. All diagnostic indices were determined for each test under consideration at the following interval from the onset of chest pain: a) 4 hours or less, b) more than 4 hours but 12 hours or less c) more than 12 hours but 24 hours or less, d) more than 24 hours after onset of chest pain. The predetermined time frames were employed after considering the release kinetics of H-FABP and similar time frames were also used in other studies (Alhashemi, 2006). All

[redacted]

INPATIENT DATA

[redacted]

Fields marked with asterisk (*)

A) Inpatient Admit Date* *(d*

B) Admit Service* *(tick only on*
(If multidisciplinary intervention, *fill in their respective surgical intervention forms)*

- ☐ Trauma/General S
- ☐ Orthopedic
- ☐ Neurosurgery
- ☐ Maxillofacial
- ☐ Cardiothoracic
- ☐ OTHER surg
- ☐ Paediatric surgical

C) Medical History*:

- ☐ Cardiac
- ☐ Neurological
- ☐ Renal Impairment
- ☐ Diabetes Mellitus
- ☐ Liver Impairment
- ☐ Respiratory
- ☐ Anticoagulant
- ☐ Immunosuppressive
- ☐ Psychiatric
- ☐ None
- ☐ Unknown

[redacted]

(Please prepare own data for p

	rt Time *h format)*	**Start Date** *(dd/mm/yyyy)*
Procedure 1	☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐
Procedure 2	☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐
Procedure 3	☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐
Procedure 4	☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐
Procedure 5	☐☐☐	☐☐ / ☐☐ / ☐☐☐☐
Procedure 6	☐☐☐	☐☐ / ☐☐ / ☐☐☐☐
Other *(specify)*:_____	☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐

study patients were sorted out into one of four time frames according to the duration of onset of their chest pain at presentation to ED. To facilitate data analysis, patients studied were categorised into 4 groups according to duration of chest pain as shown below:

Groups 1: presented to ED within 4 hours after the onset of chest pain,

Group 2: presented to ED after 4 hours but within 12 hours of chest pain,

Group 3: presented to ED after 12 hours but within 24 hours of chest pain, and

Group 4: presented to ED 24 hours after the onset of chest pain.

Sensitivity, Specificity, PPV and NPV were calculated by using Analyse-it software [Analyse-it for Microsoft Excel (version 2.11), Analyse-it Software, Ltd. **http://www.analyse-it.com/;** 2008]. Receiver operating characteristic (ROC) curve, area under curve (AUC), p-values and 95% CI were also obtained using SPSS. Inter-observer reliability (agreement between the two raters) was calculated by using Cohen's Kappa. Kappa measures and p-values were obtained. P-value of less than 0.05 was considered to be statistically significant.

CONCLUSIONS

This study has demonstrated that the qualitative CardioDetect test which detects H-FABP in the circulation was more sensitive than TnT and has a better NPV, especially during the early hours of AMI. CardioDetect test may be potentially used to rule out myocardial infarction during the early phase of ischemic chest pain. However, there are still significant rates of false negative even in the early hours of AMI, and further improvement should be made to the CardioDetect test kit.

This study concluded that repeating the CardioDetect test 1 hour after an initial negative result improved the sensitivity, specificity, PPV and NPV of the test especially during the first 4 hours after the onset of chest pain. The diagnostic accuracy of the repeat test was also more superior to the CardioDetect test alone or cardiac TnT during the early phase of chest pain. Therefore, if the initial CardioDetect test was negative, a repeat test 1 hour later is suggested, especially for patients who presents early after the onset of chest pain.

This study agreed with previous recommendations that combination tests with different release kinetics (e.g. H-FABP and TnT) improved the diagnostic performance of cardiac biomarkers in detecting AMI, as compared to performing individual test. It was shown that the combination test of CardioDetect and TnT had a better diagnostic accuracy than individual test especially during the first 4 hours after AMI. The combination test however, may be redundant as TnT test alone was proven to be adequately sensitive and specific in diagnosing AMI, except for the early hours of chest pain. The CardioDetect test was more sensitive in detecting AMI during the early hours of symptoms, and has an

added advantage of having a better NPV compared to TnT. These characteristics of CardioDetect are crucial since early exclusion of AMI depend on the sensitivity and NPV. A repeated CardioDetect test an hour later is recommended if the initial test was negative, as this was proven to have better diagnostic indices. The combination test of CardioDetect and TnT may be beneficial in selected patients such as those who present with intermittent chest pain and are unsure or unable to recall the exact time of onset of chest pain. Combining the CardioDetect and TnT would provide a wide safety net to diagnose AMI in these cases. With a high sensitivity and NPV, the combination test may be beneficial in ruling out myocardial infarction.

Despite the observed limitations in reading the qualitative CardioDetect test, the inter-observer agreement between the 2 observers was reasonably good. A comprehensive and continuous training should be incorporated to ensure accurate and proper interpretation of the CardioDetect test.

LIMITATIONS

1. The test kits were stored properly in a refrigerator in the ED at the temperature recommended by the manufacturer. However, conditions of the test kit prior to delivery were beyond our control. Initial test results of CardioDetect showed discouraging results with important and significant false negative rates being detected when compared to TnT. Inquiries and investigations revealed that the supplier did not adhere to the recommended storage temperature during transport and this may have affected the performance of the

CardioDetect test kit. The initial credit card-like CardioDetect test kit (figure 4.4a) was also stacked onto each other during packaging and the pressure load may have affected the absorbent pad and its capillary motion. Subsequent supplies of the CardioDetect test kit were made to be stored and transported properly from the manufacturer, to the supplier and in the ED. The updated version of CardioDetect test kit had a hard casing which protected the sensitive element inside (figure 4.4d).

2. The CardioDetect test kits were supplied in batches. Half way through the study, an updated version replaced the initial credit card-like test kit. The manufacturer reported that both test kit had similar characteristics including a same cut-off point for a positive test to detect H-FABP. It is not known in certainly whether the initial and updated versions of the CardioDetect test kits were comparable in all aspects.

3. The attending medical officers may be biased when reading the CardioDetect test result since they are not blinded to the history, physical examination and ECG findings of the patient being investigated. Under ideal experimental conditions, the CardioDetect test would have been a read by a separate observer who is blinded to the patient's clinical condition. However, this was not possible in a busy emergency department setting.

4. The subjective nature of the reports of the patients about the exact onset of their ischemic symptoms may potentially overestimate or underestimate the duration of their ischemic symptoms. This may have influenced the grouping of patients according to the

predetermined time frame and eventually affect the diagnostic indices of the group studied.

5. Inter-observer variability between 2 observers reading the CardioDetect test was assessed in this study. Care was taken to perform the CardioDetect test (and TnT) using standardize methods and interpretation was done in a similar environment in the ED. The CardioDetect test kit result has a tendency to change over time, and it was read at the 15 minute mark. There were instances when the second reader read the test beyond 15 minutes. This delay may have contributed to the different interpretation of the test and affected the kappa analysis to assess agreement beyond chance between the 2 readers.

6. The calculated sample size for this study was 87 patients. A total of 80 patients were enrolled. The modest number of cases recruited may have resulted in the small number of samples in certain cohorts being analysed. As a result, the repeated CardioDetect test was unable to be analysed in group 3 and 4.

ABSTRACT

Introduction

Cardiac biomarkers may be invaluable in establishing the diagnosis of acute myocardial infarction (AMI) in the ED setting.

Objective

To assess the diagnostic indices of the CardioDetect assay and the quantitative cardiac troponin T test, in diagnosing AMI in the ED, according to the time of onset of chest pain.

Methodology

A total of eighty eligible patients presenting with ischemic type chest pain with duration of symptoms within the last 36 hours were enrolled. All patients were tested for H-FABP and Troponin T at presentation to ED. A repeated Cardiodetect test was performed one hour after the initial negative result, and a repeated Troponin T test was also performed 8-12 hours after an initial negative result. The diagnostic indices [sensitivity, specificity, positive predictive value, negative predictive value, receiver operating curve (ROC)] were analysed for CardioDetect and Troponin T (individually and in combination), and also for the repeat CardioDetect test. Data entry and analysis was performed using SPSS version 12.0 and analyse-it software.

Results

The CardioDetect test was more sensitive and had a higher NPV than troponin T (TnT) test during the first 12 hours of onset of chest pain. The repeat CardioDetect had better sensitivity and NPV than the initial CardioDetect. The sensitivity and NPV of the combination test (CardioDetect and troponin T) was also superior to the each test performed individually.

Conclusion

CardioDetect test is more sensitive and has a better NPV than Troponin T during the first 12 hours of AMI. It may be used to rule out myocardial infarction during the early phase of ischemic chest pain.

Keywords: Myocardial infarction, cardiac enzymes, troponin, H-FABP

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