

Analytical Evaluation of Cardiac Poct: Humasis Hubi-Quanpro Troponin I

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ABSTRAK

Pengujian troponin melalui aplikasi point-of-care testing (POCT) adalah bertujuan untuk menambahbaik masa pengujian dan membantu dalam penjagaan dan pengurusan sindrom koronari akut. Kajian ini dijalankan untuk menilai prestasi analitikal dan korelasi HUBI-QUANPro troponin I dengan instrumen makmal sedia ada iaitu high-sensitivity troponin I, Architect Abbott. Faktor yang dikaji termasuk ujian ketepatan dengan menggunakan bahan kawalan kualiti (2 aras) dan kajian korelasi yang melibatkan perbezaan sampel (whole blood, plasma dan serum) dan metodologi (immunochromatographic dan chemiluminescent immunoassay). Sejumlah 30 bahan kualiti yang digunakan untuk kajian ketepatan dan 42 sampel serum dan EDTA untuk kajian korelasi. Tahap ketepatan adalah 10.9% dan 6.7% pada kepekatan 0.91 ng/mL dan 2.66 ng/mL. Analisis regresi bagi perbezaan sampel (plasma vs whole blood) dalam HUBI-QUANPro menunjukkan cerun 0.935, $r=0.991$ ($p<0.001$). Korelasi HUBI-QUANPro dan Architect Abbott (whole blood, plasma vs serum) mempunyai kecerunan regresi 0.205, $r=0.963$ (whole blood) dan 0.192, $r=0.954$ (plasma), $p<0.001$. HUBI-QUANPro troponin I adalah analyser yang sensitif, cepat, tepat dan mempunyai prestasi analitikal yang boleh sebanding dengan instrumen makmal bagi pengukuran troponin I jantung. Ia dapat berfungsi sebagai peranti POCT yang baik dalam pengurusan penjagaan akut berkaitan dengan masalah jantung.

Kata kunci: pengujian troponin, point-of-care testing, sindrom koronari akut

ABSTRACT

Point-of-care testing (POCT) of cardiac troponin device is aimed for improvement

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in turn round time (TAT) and assist in acute management care of acute coronary syndrome (ACS). The present study was conducted to assess the analytical performance and correlation of HUBI-QUANPro troponin I with an existing laboratory instrument of high-sensitivity troponin I, Abbott Architect. The factors that were studied, included precision study by using manufacturer quality control (QC) material (2 levels) and correlation study of sample differences (whole blood, plasma and serum) and methodology (immunochromatographic assay and chemiluminescent immunoassay). A total of 30 QC was used for precision study and 42 sample serum and EDTA for the correlation study. An acceptable total imprecision of 10.9% and 6.7% were seen at level of 0.91 ng/mL and 2.66 ng/mL, respectively. Regression analysis of sample differences (plasma vs whole blood) in HUBI-QUANPro showed slope of 0.935, $r=0.991$ ($p<0.001$). Correlation of HUBI-QUANPro and Abbott Architect (whole blood, plasma vs serum) both demonstrated regression slope of 0.205, $r=0.963$ (whole blood) and slope of 0.192, $r=0.954$ (plasma), $p<0.001$, respectively. HUBI-QUANPro troponin I POCT device is a sensitive, fast, precise and has a good comparable analytical performance with reference laboratory instrument for cardiac troponin I measurement. It is able to serve as a good POCT device in cardiac-related acute care management.

Keywords: *acute coronary syndrome, cardiac troponin I, point-of-care testing*

INTRODUCTION

Acute coronary syndrome (ACS) is a clinical spectrum from ST-elevation myocardial infarction (STEMI) to Non-ST elevation myocardial infarction (NSTEMI) and unstable angina (UA). Worldwide, ACS remains an important cause of morbidity and mortality. In Malaysia, STEMI was the commonest subtype as compared to NSTEMI-UA and commonest in the young patients below the age of 50 years (Yip et al. 2017). The distinguishable pattern of NSTEMI and UA was able to be discriminated, based on the presence of troponin cardiac biomarkers. Thus, the demonstration of troponin is extremely important in the diagnosis and management of the patient.

Fast administration of treatment of less than 1 hour is beneficial in ensuring of good outcome of ACS patients (Hamm et al. 2011; Van de Werf et al. 2008). Made availability of the measurement of cardiac troponin in less than 60 minutes in the Emergency Department, contributes a lot to the acute management of ACS (Storrow et al. 2006). Most central laboratories unable to meet the 60-minute turn around time (TAT) for troponin measurement. Based on National Academy of Clinical Biochemistry (NACB) with regard to practice for point of care; Guideline 18: institutions that cannot consistently deliver cardiac marker TAT of 60 minutes, should implement point-of-care testing (POCT) devices (Storrow et al. 2006).

POCT is defined as any diagnostic test that is performed at or close to the location of a patient that has the ability to provide improvement in TAT of a test result and help in expediting medical decision-making, improvement in health care management and provide benefit both patient and clinical care provider. In relation of cardiovascular utility, POCT enable high-quality biomarker measurements that is to optimize for suitability of diverse clinical setting including acute care, out-patient clinics, and clinical research centres. POCT for troponin has been available for about 2 decades and with its utility in Emergency Department for patients presenting with ischemia symptoms can be appropriately triage and received proper treatment (King et al. 2016). Cardiac troponin POCT performance specifications and characteristics should not differ from the central laboratory (Larsson et al. 2015). The cardiac troponin POCT device should meet a 10% coefficient variation (CV) at the 99th percentile (Amundson & Apple 2015).

HUBI-QUANpro is a movable POCT device, complete and simple cartridge reader. It is developed to provide a rapid quantitative result for a membrane-based lateral flow immunochromatographic assays. It allows concurrent diagnosis up to six different markers in 15 minutes interval, inclusive of Troponin I biomarker. HUBI-QUANpro troponin I was designed for quantitative measurement of cardiac Troponin I in human whole blood or plasma. HUBI-QUANpro troponin I is useful in providing fast decision making in the Emergency

Department, clinical wards, and critical care settings.

The study was conducted to evaluate and validate the performance claim of HUBI-QUANpro troponin I (POCT) by manufacturer and correlation of HUBI-QUANpro analyzer with existing chemistry analyzer Abbott Architect i2000SR in Chemical Pathology Laboratory, Universiti Kebangsaan Malaysia Medical Centre (UKMMC) as well as to assess the suitability of HUBI-QUANpro analyzer for cardiology POCT.

MATERIALS AND METHODS

Assays Method

The HUBI-QUANPro POCT device is from HUMASIS, Gyeonggi-do, South Korea. It is a single-use one-step immunoassay device with a reflectance image sensor that was designed to determine the concentration of cardiac troponin I in the whole blood or plasma specimen. The test procedure involved pipetting 100 uL of blood specimen to the sample test well on the device. The specimen acts with colloidal gold antibody conjugates and flows through the test device via capillary action. Complexes of each sample and colloidal gold antibody conjugate are captured on a discrete zone resulted as a binding assay. The cardiac troponin I value in the specimen is directly proportional to the reflectance image detected. A larger amount of density on the reflectance image indicates a higher cardiac troponin I concentration. The result availability is approximately 15 minutes. The limit of detection is <

0.05 ng/mL with measuring range of 0.05-20 ng/mL. The diagnosis cut-off (positivity) is 0.4 ng/mL.

Routine serum high-sensitivity troponin I (hs-troponin I) measurements were performed on Abbott Architect i2000SR from Germany. The analyzer utilized two-step immunoassay using chemiluminescent immunoassay (CMIA) principle for troponin I measurement. The chemiluminescent reaction is measured as relative light unit (RLU) and the value of cardiac troponin I concentration is directly proportional with RLU. Analytical precision (within and total CV) of hs-troponin I for Abbott Architect was less than 5% for 3 level quality control (QC) value.

Strict quality assurance protocols were performed for both assays. Standardization of HUBI-QUANPro quality material was using refined protein preparation of Troponin I that was established on the mass (concentration) of analyte that presents in EDTA plasma.

Precision Study

The study was conducted on HUBI-QUANPro POCT device according to CLSI EP15-A2 Guideline using manufacturer QC material that covers two different levels and medical decision limit. The QC material was analyzed in triplicate for each level for five days and all data was recorded in within and total CV. The obtained CV was compared with the manufacturer's claim CV.

Correlation Study

The study consisted of two correlation assessments that looked at the sample differences as well as the assays method. A total of 42 samples of serum and EDTA (whole blood and plasma) were used in the study. The samples were randomly selected in the laboratory based on availability of request for hs-troponin (serum sample) and full blood count (FBC) for EDTA sample collection irrespective of the diagnosis. A comparison of sample differences between whole blood and plasma was conducted on the HUBI-QUANPro. The data was compared with the serum result of cardiac troponin from Abbott Architect i2000SR analyzer. The EDTA samples were analyzed for cardiac troponin I value within the stability period of 2-hours at room temperature. The correlation of each comparison was evaluated according to CLSI EP 9A guideline.

Statistical Analysis

The imprecision of the HUBI-QUANPro cardiac troponin I POCT reader were expressed in mean and CV of within-run and total imprecision. Analysis ToolPak for Microsoft Excel, Office 16 was used for linear regression analysis of the comparative study of different sample material on HUBI-QUANPro cardiac troponin I and different methods of HUBI-QUANPro and Abbott Architect i2000SR. All regression analysis was expressed as slope (m), intercept, correlation coefficient (r), and coefficient of determination (R^2). The slope represents proportional bias while intercept is a reflect of constant

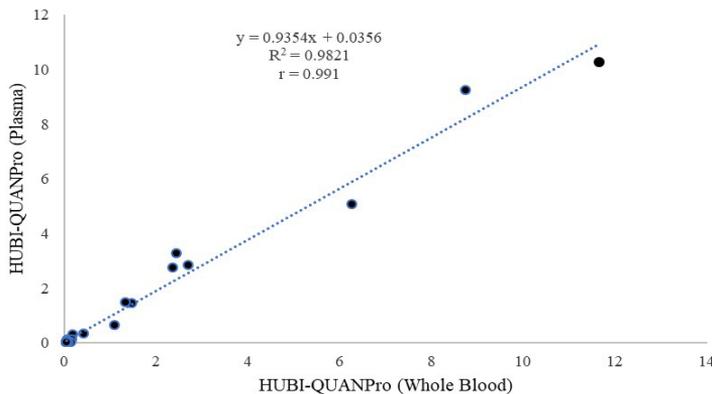


Figure 1: Linear regression analysis of HUBI-QUANPro Cardiac Troponin I of whole blood and plasma sample.

bias. r value is a measure of association strength of two variables which value lies in between -1 to 1 signify good or strong linear relationship while R² value is used to describe the fairness of distribution of observed data in the linear regression analysis. The value of 1 implies that the dependent variable can be predicted from the independent variable. The Bland-Altman plots were used for illustration of a comparison of the correlation between different sample measurements and between HUBI-QUANPro and Abbott Architect i2000SR at the central laboratory.

RESULTS

PRECISION STUDY

A total of 30 data was collected for

both level 1 and level 2 in the precision study. The mean for level 1 and level 2 were 0.91 ng/mL and 2.66 ng/mL, respectively. The within-run and total imprecision for both QC levels were within the manufacturer’s claim. The precision study of HUBI-QUANPro Cardiac Troponin I was acceptable. (Table 1).

COMPARISON/CORRELATION STUDY

Sample comparison on HUBI-QUANPro Cardiac Troponin I (Whole blood and Plasma)

The slope generated for sample comparison of whole blood and plasma on HUBI-QUANPro Cardiac Troponin I was 0.9354 (95% CI: 0.8951-0.9757, p<0.001) and the coefficient

Table 1: Precision Study of HUBI-QUANPro Cardiac Troponin I

Level	Mean (ng/mL)	Within-run Imprecision (%)	Claim Within-run Imprecision (%)	Total Imprecision (%)	Claim Total Imprecision (%)
1- Low	0.91	13.3	14.01	10.9	15.33
2- High	2.66	8.2	9.16	6.7	13.43

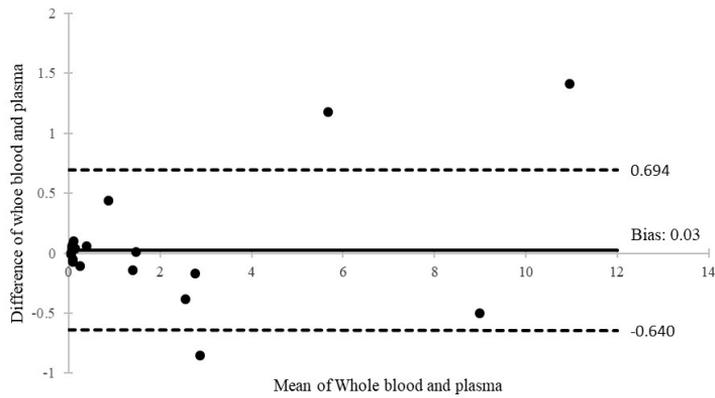


Figure 2: Bland-Altman plot HUBI-QUANPro Cardiac Troponin I of whole blood and plasma

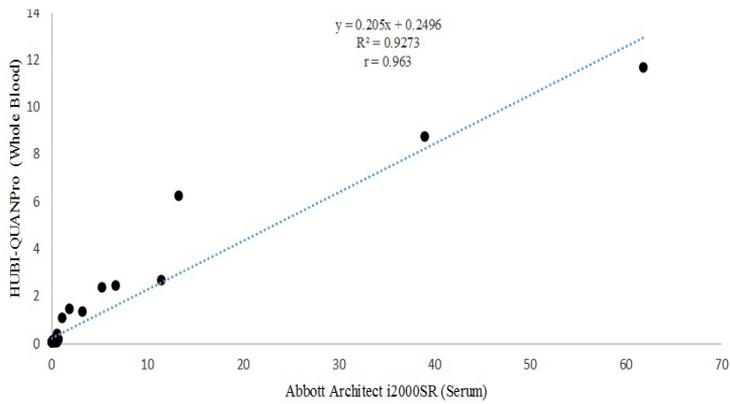


Figure 3: Linear regression analysis of HUBI-QUANPro Cardiac Troponin I (whole blood) with Abbott Architect i2000SR (serum).

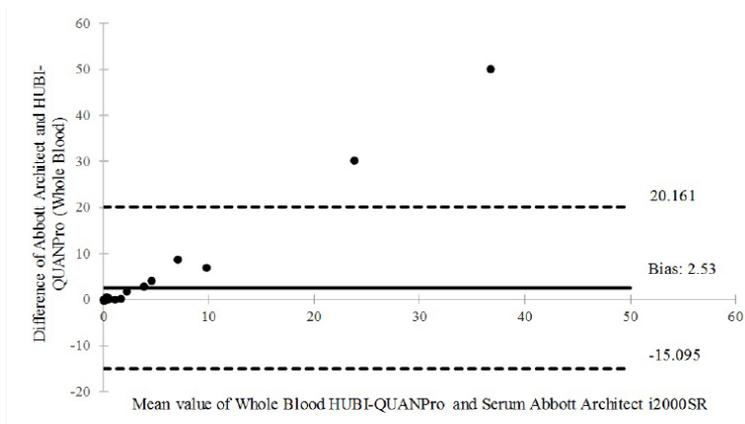


Figure 4: Bland-Altman plot HUBI-QUANPro Cardiac Troponin I (whole blood) and Abbott Architect i2000SR (serum).

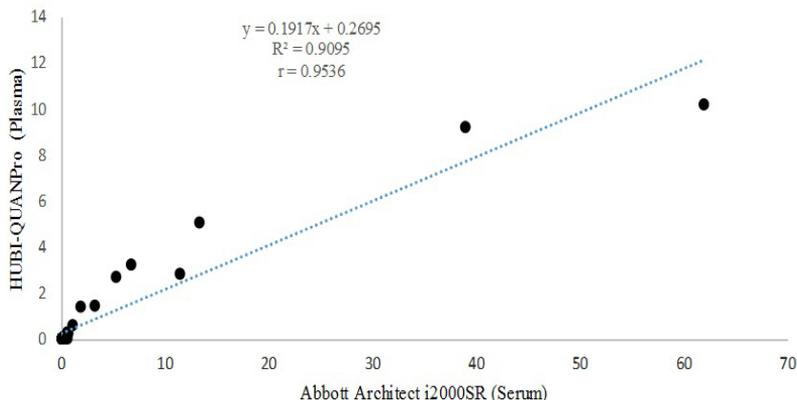


Figure 5: Linear regression analysis of HUBI-QUANPro Cardiac Troponin I (plasma) with Abbott Architect i2000SR (serum).

correlation (r) was 0.991 (Figure 1). The average bias for measurement of cardiac Troponin I in both whole blood and plasma was 0.03 ng/mL (CI 95%: - 0.640-0.694) (Figure 2).

Comparison between HUBI-QUANPro Cardiac Troponin I (Whole blood) with Abbott Architect i2000SR (Serum)

The slope attained from the comparison of analytical results for the HUBI-QUANPro whole blood samples and serum result of Abbott Architect i2000SR at the central laboratory was 0.205 (95% CI: 0.1867-0.2234, $p < 0.001$) and the coefficient correlation (r) was 0.963 (Figure 3). The average bias for measurement of cardiac Troponin I in both whole blood and serum was 2.53 ng/mL (CI 95%: - 15.095-20.161) (Figure 4).

Comparison between HUBI-QUANPro Cardiac Troponin I (Plasma) with Abbott Architect i2000SR (Serum)

The slope obtained from the comparison of cardiac Troponin I in plasma using HUBI-QUANPro and serum sample by Abbott Architect i2000SR was 0.1917 (95% CI: 0.1724-0.2109, $p < 0.001$) and the coefficient correlation (r) was 0.9536 (Figure 5). The average bias for measurement of cardiac Troponin I in both whole blood and serum was 2.56 ng/mL (CI 95%: -15.368-20.487) (Figure 6).

Table 2 summarizes the correlation between different sample analysis on HUBI-QUANPro Cardiac Troponin I reader and with the central laboratory analyzer of Abbott Architect i2000SR.

DISCUSSION

The POCT system is the appropriate way of test for rapid evaluation of patient presenting with acute coronary syndrome (Juliano & Wason 2017). According to the results, it is proven that HUBI-QUANPro troponin I was able to provide result at ~15 minutes interval which meets the POCT advantages of providing cardiac

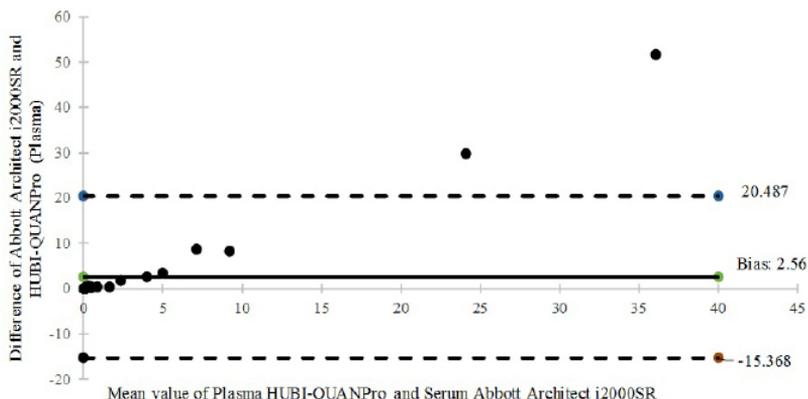


Figure 6: Bland-Altman plot HUBI-QUANPro Cardiac Troponin I (plasma) and Abbott Architect i2000SR (serum).

troponin result at shorter interval that has potential in improving the acute patient care and enabling rapid clinical decision. The quantification of cardiac troponin in HUBI-QUANPro is made to analyze whole blood and plasma (EDTA) sample and it needs no sample preparation which able to reduce the user or handler error and turnaround time.

HUBI-QUANPro troponin I has an acceptable within and between run precision for both quality control levels. Thus, it meets the claimed imprecision. However, for low level control, even though it has acceptable imprecision, the mean value is 0.91

ng/mL and it lies in the third standard deviation (3SD) of control range as compare to the manufacturer claimed for it low mean of 0.65 ng/mL (2SD). It is important to highlight this as the cut off for diagnosis being made is 0.4 ng/mL and this value is within 2SD control range. To note that prior to precision study conducted, the internal quality control was acceptable for low level thus the fluctuation of the precision study results may be due to improper handling of the control material according to the manual for user.

As HUBI-QUANP troponin I POCT able to analyze both whole blood and plasma sample, we conducted

Table 2: Correlation results of HUBI-QUANPro and AbbottArchitect i2000SR

	Regression Equation	r	Mean Bias	p -value
HUBI-QUANPro Whole blood vs Plasma	$y = 0.9354x + 0.0356$	0.991	0.03	< 0.001
HUBI-QUANPro (whole blood) vs Abbott Architect i2000SR (serum)	$y = 0.205x + 0.2496$	0.963	2.53	< 0.001
HUBI-QUANPro (plasma) vs Abbott Architect i2000SR (serum)	$y = 0.1917 + 0.2695$	0.954	2.56	< 0.001

the correlation study on both matrixes that was expressed as coefficient correlation and bias based on linear regression analysis and Bland-Altman plot respectively. The correlation coefficient (r) were classified as very high ($r=0.90-1.00$), high ($r=0.70-0.89$), and moderate ($r=0.50-0.69$) (Zady et al. 2000). Based on the study, there is very high correlation ($r=0.991$) with minimal bias of 0.03 ng/mL in different matrix studied that is highly significant, $p<0.001$. The finding justified the use of either sample of whole blood or plasma on HUBI-QUANPro troponin I.

Both whole blood and plasma sample were found to have very high correlation with similar mean bias of 2.5 ng/mL (whole blood, $r=0.963$, plasma, $r=0.954$, $p<0.001$) with laboratory high-sensitivity Troponin I (serum) by Architect Abbott. The analytical correlation of HUBI-QUANPro and Architect Abbott ($n=42$), were almost similar to the comparison between HUBI-QUANPro and ADVIA Centaur XP troponin I ($r=0.956$) that was obtained from the HUBI-QUANPro POCT device information for user. Analytical performance evaluation of POCT analyzer is an essential first step in the selection of appropriate instruments for POCT applications (Boonlert et al. 2003). Ideally, the analytical performance of a POCT device for cardiac troponin should not differ from that provided by the central laboratory system (Kemper et al. 2017). The study may have limitations as there were small number of testing samples for the correlation ($n= 42$) and it was conducted by trained laboratory staff

instead of average POCT personnel. The study should be explored on the analytical evaluation of testing the potential interference substances, detection limit, linearity, reference cut-off and clinical evaluation.

CONCLUSION

HUBI-QUANPro troponin I POCT device is a sensitive, fast, precise and has a good comparable analytical performance with reference laboratory instrument for cardiac troponin I measurement. It is able to serve as a good POCT device in cardiac related acute care management.

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