There was a significant increase in serum concentration of MDA in hypertensive subjects (p<0.05) when compared with normotensive subjects. The significant increase in serum concentration of MDA in hypertensive subjects (p<0.05) suggest lipid peroxidative activity involvement in the etiology of hypertension. Serum level of superoxide dismutase (SOD), catalase (CAT) and reduced glutathione (GSH) significant reduction in hypertensive subjects irrespective of gender suggest their involvement in the neutralization of free radicals that has been linked with the pathogenesis of hypertension.

The NT-proBNP level in Subclinical stage of cardiac structural or functional abnormalities among health checkups

E. Nah1, S. Kim2, S. Cho3, S. Kim4. 'Korea association of Heath Promotion, Health Promotion Research Institute, Seoul, Korea, Republic of; 'Korea association of Heath Promotion, Division of Cardiology, Department of Internal Medicine, Seoul, Korea, Republic of

Background: The heart failure stage B is defined as patients with abnormal heart structure/function without symptoms. Circulating concentration of NT-proBNP is raised in symptomatic patients with left ventricular (LV) dysfunction which caused by structural or functional Impairment. This study performed to investigate the association of NT-proBNP level with echo-defined cardiac structural or functional (diastolic) anomalies in asymptomatic subjects with preserved LV function (ejection fraction >50%).

Methods: We retrospectively studied 412 health examinees who underwent echo-cardiography and NT-proBNP test at a health promotion center in Seoul, between January 2016 and December 2016. Increased left ventricular mass index (LVMI), and left atrial dimension (LAD) were used as markers of structural anomalies, and septal e' velocity and E/e' were used as markers of diastolic dysfunction. NT-proBNP was measured by electrochemiluminescence immunoassay (Siemens Healthcare Diagnostics, DPC Immulite 2000 XiP, Tarrytown, NY, USA).

Results: Multivariate regression analysis indicated that the factors associated with higher NT-proBNP were older age, female sex, lower BMI, lower blood pressure, higher creatinine, and higher LAD. The NT-proBNP levels were higher with increasing age groups, lowest in those aged ≤45 years and highest in those aged >60 years (P<0.001). While female in those aged ≤50 years demonstrated higher NT-proBNP levels than males (P=0.001), there was no significant difference of NT-proBNP levels in those aged >60 years. The structural anomalies, which were defined increased LVMI or LAD, demonstrated higher NT-proBNP than normal LVMI and LAD (P<0.05). However, diastolic dysfunction, which was defined decreased septal e' velocity or increased E/e' was not associated with NT-proBNP level.

Conclusion: The level of NT-proBNP was associated with subclinical cardiac structural anomalies but not associated with diastolic dysfunction in asymptomatic health checkups.

Diagnostic performance of copeptin for acute myocardial infarction in emergency department

P. Park, J. Jeong, K. Chun. Gachon medical school Gil medical center, Incheon-shi, Korea, Republic of

Background: The aim of this study was to investigate the effectiveness of copeptin in the diagnosis of acute myocardial infarction (AMI), and to compare the diagnostic performance of copeptin with other cardiac markers. Methods: We prospectively enrolled 293 patients presenting with chest pain (onset within 12 hours) suggestive of acute coronary syndrome (ACS) to the emergency department. Serum CK-MB, troponin I and copeptin levels were measured in each patient and were compared between ACS groups for statistical differences. The accuracies troponin I, CK-MB and copeptin for AMI diagnosis were assessed by ROC curve analysis. The performance of each marker and combination of three markers is assessed by comparing their AUCs. And diagnostic performance of three markers was analyzed to onset of chest pain. Results: Median age was 60 years; 70.0 % were men; 24.6% were unstable angina and 134 other diseases. The combination of three markers (AUC: 0.980, 95% CI: 0.957-0.993) had better diagnostic performance for AMI than troponin I (AUC: 0.801, 95% CI: 0.750-0.840) or CK-MB (AUC: 0.758, 95% CI: 0.705-0.806) or copeptin (AUC: 0.796. 95% CI: 0.745-0.840) alone (P<0.001). And the combination of three markers (AUC: 0.902, 95% CI: 0.862-0.934) had better diagnostic accuracy for STEMI than troponin I (AUC: 0.744, 95% CI: 0.690-0.793) or CK-MB (AUC: 0.676, 95% CI: 0.619-0.729) or copeptin (AUC: 0.844, 95% CI: 0.797-0.884) alone (P<0.001). The use of three respective of gender (p< 0.05) when compared with normotensive subjects.

Conclusion

The significant increase in serum concentration of MDA in hypertensive subjects (p<0.05) suggest lipid peroxidative activity involvement in the etiology of hypertension. Serum level of superoxide dismutase (SOD), catalase (CAT) and reduced glutathione (GSH) significant reduction in hypertensive subjects irrespective of gender suggest their involvement in the neutralization of free radicals that has been linked with the pathogenesis of hypertension.

Cardiac Markers

S. Radah. Berkeley Heart Lab, Alameda, CA

Over the past several decades, numerous studies have established that increased levels of apolipoprotein(a) [Lp(a)] in plasma are associated with development of coronary heart disease (CHD). Upon discovery of the apo(a) gene (LPA), it was considered one of the most polymorphic transcribed genes in the human genome, researchers reported several polymorphism in LPA gene which associated with CHD and plasma Lp(a) levels. Recently, a single nucleotide polymorphism (SNP) rs3798220, also known as Ile4399Met, encoding an isoleucine to methionine substitution located in the protease-like domain of apo(a) at amino acid 4399 have been shown to be associated with CHD and plasma Lp(a) levels in Caucasians. This study investigated the association of SNP rs3798220 with plasma Lp(a) in a large scale of Berkeley HeartLab samples representing genetically diverse populations. The study showed that the heterozygous carriers of SNP rs3798220 (Ile/Met) had 2.8 fold higher serum Lp(a) levels with a mean of 64.3 mg/dL and 95% CI [63.1, 65.5] (p = 0.0000) compare to serum Lp(a) levels of homozygous non-carriers (Ile/Ile) having a mean of 33.4mg/dL and 95% CI [33.0, 33.6]. Interestingly, this study showed that the homozgyous carriers (Met/Met) have 2.1 fold lower plasma Lp(a) than non-carriers (Ile/Ile) with a mean of 24.5mg/dL. (p = 0.0034) and 6 fold lower than heterozygous carries (Ile/Met). This study also investigated the association of the same SNP with other biomarkers and concluded that there was a strong and clinically significant association between carriers of Ile/Met (genotype ag) and Met/Met (genotype gg) with high serum Triglyceride levels.

A-066

Study On Lipid Peroxidation & Enzymatic Antioxidant Activities In Hypertensive Subjects

A. T. Opundajo. Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife, Osun State, Nigeria

Background

Lipid peroxidation is a degenerative process that affects cell membranes and other lipid containing structures under conditions of oxidative stress which is an essential early event in the pathogenesis of atherosclerosis as a major complication of hypertension. Hypertension is a major public health challenge; a major risk factor for cardiovascular disorder especially essential hypertension characterized by sustained elevation of blood pressure without any identifiable cause. Hypertension is a major public health challenge; a major risk factor for cardiovascular disorder especially essential hypertension characterized by sustained elevation of blood pressure without any identifiable cause. This study investigates the generation lipid peroxidation product (malonaldehyde) and its effects on physiological catalase, reduced glutathione (GSH) significant reduction in hypertensive subjects ir-
Cardiac Markers

markers also showed superior performance for NSTE MI than troponin I (AUC: 0.779, 95% CI: 0.727-0.825) or CK-MB (AUC: 0.782, 95% CI: 0.730-0.838) or troponin (AUC: 0.642, 95% CI: 0.584-0.697) alone. In patients with onset of chest pain less than 1 hour (1hr group), troponin was most superior to other markers in diagnosis of AMI (AUC: copetin-0.739, CK-MB-0.620, troponin-1-0.595, comparison of AUC: Copetin vs CK-MB: P<0.008, Copetin vs troponin I: P<0.003). In group with onset of chest pain less than 2 hours (2hr group), troponin showed better performance than troponin I for AMI diagnosis (AUC: copetin-0.732, CK-MB-0.642, troponin-1-0.609, comparison of AUC: Copetin vs troponin I: P<0.009). The result of separating group showed that troponin was best marker for early diagnosis to STEMl (comparison of AUC in 1hr group: Copetin vs CK-MB: P<0.001, Copetin vs troponin I: P<0.002/ comparison of AUC in 2hr group: Copetin vs CK-MB: P<0.001, Copetin vs troponin I: P<0.001). However, there was no difference in diagnostic performance according to onset of chest pain in NSTEMI group. And copetin showed higher negative predictive value than other markers in STEMl patients (copetin-0.96.71 (95% CI: 92.78-98.54), troponin I- 88.97 (95% CI: 86.85-90.79), CK-MB-89.39 (95% CI: 86.92-91.44). Conclusion: In chest pain patients, combination of copetin addition to troponin I and CK-MB improves AMI diagnostic performance. And copetin especially helps in early diagnosis and rule-out of STEMl patients.

A-069

Early detection of doxorubicin-induced cardiotoxicity with high-sensitivity troponin T in chemotherapy-treated patients

J. Li1, J. Banchs2, P. Vejpongsa3, D. M. Araujo4, E. A. Wagner1, E. T. H. Yeh5, Q. H. Meng6, E. T. H. Yeh1, Q. H. Meng1, E. T. H. Yeh1, Q. H. Meng1, E. T. H. Yeh1, Q. H. Meng6, 1MD Anderson Cancer Center, Houston, TX, 2University of Texas McGovern School of Medicine, Houston, TX, 3University of Missouri School of Medicine, Columbia, MO

Background: Detection of chemotherapy-induced cardiotoxicity has historically relied on clinical presentation and cardiac imaging measures. Recently, global longitudinal peak systolic strain (GLS) measures with speckle tracking echocardiography (STE) and high-sensitivity troponin T (hs-TnT) have been utilized to evaluate the development of cardiotoxicity. The increased sensitivity of these methods may allow us to detect early development of cardiotoxicity and predict future cardiac dysfunction in chemotherapy-treated patients. We investigated the effectiveness of hs-TnT and GLS in detecting doxorubicin-induced cardiotoxicity.

Methods: Thirty-six patients with newly diagnosed sarcoma were assigned to receive 72-hours doxorubicin infusion. hs-TnT was monitored before, and at 72 hours of each chemotherapy cycle. All samples were assayed at the same time using hs-TnT (Roche diagnostics). Elevated troponin was defined as hs-TnT > 5 ng/L. STE was performed pretreatment, after cycle 3, and end of chemotherapy. Only patients who received ≥ 150 mg/m2 of doxorubicin and had at least two STE were included for evaluation of GLS and left ventricular ejection fraction (LVEF).

Results: Six patients (25%) developed cardiotoxicity as defined by a decline in LVEF >10% by the Cardiac Review and Evaluation Committee. The absolute levels of hs-TnT had significantly peaked from precycle baseline, increased starting at cycle 2, subsequently in each precycle and during the cycle of therapy (p<0.05). Fold changes over baseline in-hs-TnT level were also significantly increased. In all six patients with cardiotoxicity, GLS increased significantly at the end of chemotherapy, compared with baseline (21.2±1.1% vs -19.2±2%). The increase in GLS by 15% and hs-TnT by 5ng/L were independent predictors of the development of cardiotoxicity at the end of chemotherapy (p<0.05).

Conclusion: In conclusion, hs-TnT and GLS predict the development of cardiotoxicity in patients treated with doxorubicin. These two parameters may be useful in predicting and detecting the development of chemotherapy-induced cardiotoxicity and thus reduction of the incidence of its associated morbidity and mortality.

A-070

Comparison of analytical outlier rates between Roche 4th and 5th generation Troponin T assays using both serum and plasma samples


Background: Analytical outliers occur with most troponin methods and can adversely affect patient management. Because higher sensitivity troponin reagents result in more troponin values that exceed the 99th percentile value, it may be difficult to identify these analytical outliers. In this study, we compared the analytical outlier rates of the Roche 4th generation Troponin T STAT (cTnT Gen 4) and Roche 5th generation Troponin T STAT (cTnT Gen 5) assays using both serum and plasma samples.

Methods:

Paired rapid clot serum tubes (RST) and plasma separator tubes (PST) (N=1426 pairs) were collected from hospital patients with orders for clinical cTnT testing. RST and PST samples were centrifuged for 3 minutes at 4000 x g for 3 minutes, and re-analyzed on both Gen 4 and Gen 5 methods. We defined analytical outliers as:

- Initial and repeat results differing on the cTnT Gen 4 assay by >0.03 ng/dL for results <0.20 ng/mL or >20% for results ≥0.20 ng/mL.
- Initial and repeat results differing on the cTnT Gen 5 assay by >10 ng/mL for results <100 ng/L or ≥10% for results ≥100 ng/L.

We also calculated the number/percent of repeat values that were on different sides of the 99th percentile upper reference limit (URL) for each assay.

Results: Using the cTnT Gen 4 assay, 379/1426 (26.6%) and 391/1426 (27.4%) PST results were above the 99th percentile of ≥0.01 ng/mL. Using sex-specific 99th percentile cut-offs on the cTnT Gen 5 assay of >10 ng/L (females) and >15 ng/L (males), 809/1426 (56.7%) RST and 802/1426 (56.2%) PST results were above the 99th percentile. For cTnT Gen 4, 6/8115 (0.06%) RST and 8/8115 (0.07%) PST samples analyzed resulted in analytical outliers all of which were within ±10% of the 99th percentile URL. For cTnT Gen 5, we observed analytical outliers in 10/8115 (0.8%) RST and 10/8115 (0.8%) PST samples. However 15% of Gen 5 outliers had repeat values on different sides of the 99th percentile URL. For both Gen 4 and Gen 5 reagents, 50% of outliers had higher TnT results upon repeat testing while 50% had lower results.

Conclusion: Analytical outliers occur frequently (0.5-1.0% of samples) with both Gen 4 and Gen 5 cTnT assays independent of sample type. No outlier results occurred on different sides of the 99th percentile URL for Gen 4. 5th Gen cTnT had a similar outlier rate but more were relevant to the determination of an elevated value. Compared to 4th Gen cTnT, use of 5th Gen cTnT will increase the percent of patients with elevated (above 99th percentile URL) values without reducing the rate of analytical outliers.

A-071

Comparison of the sensitivity and specificity of the RAMP® Troponin I assay and ADVIA Centaur® Tnl-Ultra Assay

J. F. Wilson1, S. Moran1, E. Sears2, J. Giancarlo2, V. Luzzi3, 1Response Biomedical Corp., Vancouver, BC, Canada, 2Providence Health and Services, Portland, OR

Background: Measurement of cardiac troponin I (Tnl) aids in the diagnosis of acute myocardial infarction (AMI) and in the prioritization of patient management. The purpose of this study was to compare the sensitivity and specificity of the RAMP® Troponin I assay on the RAMP 200 instrument and ADVIA Cen taur® Tnl-Ultra Assay on the ADVIA Centaur CP instrument1. The ADVIA Cen taur CP System is a mid-volume, high throughput bench top laboratory instrument with chemiluminescent technology. The RAMP system is a lateral flow fluorescent immunoassay platform with a smaller footprint. Testing was performed over two days in the laboratory of a large urban hospital in Portland, OR.

Methods: Paired lithium heparin plasma and EDTA whole blood samples were used for this study. Specimens were selected by medical laboratory staff based on the ADVIA Centaur CP Troponin I result listed in the laboratory information system, de-identified, and provided to study personnel. Lithium heparin plasma samples were retested on the ADVIA Centaur CP concurrently with EDTA blood samples on the RAMP system. Results were compared between instruments, and to the patient diagnosis as determined from the electronic medical record by medical staff.

Results: EDTA RAMP results were compared to the original lithium heparin Centaur results. Retesting of lithium heparin specimens in the Centaur CP was not reliable due to the presence of fibrin clots in the original specimens. A total of 74 samples were included in this study; 2 samples were excluded due to specimen age (>12 hours elapsed since original testing) and 1 sample was excluded due to an error during sampling. The RAMP Troponin I and ADVIA Centaur Tnl-Ultra Assay results showed 97% concordance. Using the 99th percentile as a cutoff, the RAMP Troponin I test (< 0.10 ng/mL) showed comparable sensitivity and specificity, 81% and 91% respectively, to the Advia Centaur Tnl-Ultra Assay (< 0.04 ng/mL), 75% and 91% respectively, when compared to the electronic medical record (i.e. ECG result). Also comparable were the positive predictive values (PPV), 84% and 84%, and negative predictive values (NPV), 89% and 85%, for the RAMP and Centaur systems respectively.

Conclusion: The possibility of using the RAMP Troponin I test at immediate and urgent care facilities is very attractive. Both the RAMP Troponin I test...
and the ADVIA Centaur Tnl-Ultra Assay showed excellent specificity, when used in conjunction with other clinical findings (e.g. abnormal ECG), in the diagnosis (rule-in) of AMI. The results of the study therefore support the use of the RAMP Troponin I test on the RAMP 200 system as an alternative to the larger laboratory systems, where maintenance and calibration downtime, limited space, or lower volumes would necessitate a smaller, yet effective option. Both devices are available for sale in the US and are CE Marked.

A-072

Single Molecule Technology: Equivalence between a research platform and a CE-marked diagnostic platform for the quantification of cardiac troponin I

J. Estis, P. Katzenbach, J. Sandlund, L. Monsalve, R. Livingston, A. Bartolome, J. Bishop. Singulex, Alameda, CA

Background: Single Molecule Counting technology has enabled the quantification of intractable low-abundance biomarkers. The Erenna® Instrument (research use only, RUO) and the CE-marked diagnostic Singulex Clarity® system are powered by Single Molecule Technology. Numerous studies have generated clinically important information on RUO-based platforms, but their translatability to clinically useful platforms has not been demonstrated. In this study, the correlation and equivalence of the Singulex Clarity system and the Erenna Instrument for measurements of cardiac troponin I (cTnI) were evaluated.

Methods: De-identified EDTA-plasma samples (n = 120) were first tested by the Singulex Clarity® cTnI assay on the Singulex Clarity system (limit of quantification 0.14 pg/mL) and subsequently measured on the Erenna Instrument. The study on frozen samples, biobanked from a CLIA-licensed clinical lab, were selected to span a wide range of the assay. Passing-Bablok and Pearson’s R correlation analyses were performed to compare and quantify the linear relationship between the assays.

Results: cTnI was measured in all samples and the concentrations ranged from 0.54 to 102.03 pg/mL, as measured by the Singulex Clarity system. When comparing the Singulex Clarity system and the Erenna Instrument, the Pearson correlation coefficient was 0.99 (95% CI: 0.99-1.00; Figure), indicating nearly all the variance in the Singulex Clarity results could be explained by the Erenna results. The coefficient from the Passing-Bablok regression was 0.85 (95% CI: 0.82-0.89), indicating a slight bias between the two instruments that may be explained by standardization differences.

Conclusion: The Singulex Clarity cTnI assay on the Singulex Clarity system had good correlation with the Erenna Instrument for cTnI measurements in EDTA plasma, as indicated by a strong linearity relationship between the platforms. The systems provided substantially equivalent results, demonstrating that findings on cTnI measurements using the Erenna Instrument are equivalent to those obtained using the Singulex Clarity system.

A-073

Performance Evaluation of Atellica IM High-Sensitivity Troponin I Assay in a Clinical Chemistry Laboratory

T. Fasano, R. Alcotti, L. Tondelli, R. D’Andrea, L. Vecchia. Clinical Chemistry and Endocrinology Laboratory, Department of Diagnostic Imaging and Laboratory Medicine, Arcispedale Santa Maria Nuova – IRCCS, AUSL Reggio Emilia, Italy, Reggio Emilia, Italy

Background: Cardiac troponins have become the preferred biomarker for diagnosis of MI. As sensitivity of troponin assays has increased, so has the precision at the lower end, shortening time points between serial measurements, and improving the sensitivity for early detection of MI. The Atellica® IM High-Sensitivity Troponin I (TnIH) Assay* is an in vitro diagnostic immunoassay for the quantitative determination of cardiac troponin I in serum or plasma. The objective of this study was to verify the analytical performance (precision and linearity) of the Siemens Healthineers Atellica IM TnIH Assay on the Atellica® IM 1600 Analyzer, and perform method comparison with the ADVIA Centaur® High-Sensitivity Troponin I (TNIH) Assay. (*Not available for sale in the U.S. Future availability cannot be guaranteed.)

Methods: The Atellica IM TnIH Assay is a dual-capture sandwich immunoassay using magnetic latex particles, a proprietary acridinium ester for chemiluminescence detection, and three monoclonal antibodies. The precision studies were evaluated according to EP05-A3 and EP15-A2 and method comparison to EP09-A3. Precision studies used lithium heparin plasma samples, two sample pools, and three levels of controls. One aliquot of each sample pool and each QC material was tested in replicate in two runs per day on each analyzer for a minimum of ten days with one lot of reagent and calibrator. Each run was separated by approximately a two-hour time interval. A total minimum of 40 replicates were generated per sample. Serial measurements were obtained for lithium heparin samples from >50 chest pain Emergency Department patients. Troponin samples at admission and 1, or 2, or 3, or up to 6 h later were analyzed using the Atellica IM TnIH
Cardiac Markers

Assay, and the ADVIA Centaur TnIH assay. Siemens Healthineers supported the study by providing systems, reagents and protocols and contributed to data analysis.

Results: Precision studies agreed with the manufacturer’s claims: Within day CV(%SD)Js were 5.4(0.61), 4.1(0.4), 2.1(0.79), 1.9(6.73), 1.8(3.258) for concentrations of 11.4, 25.4, 37.1, 349.72, 18056.4 ng/g/ml; within lab (total) CV(%SD)Js were 6.9(0.79), 4.4(1.12), 3.4(1.27), 3.0(104.48), 2.4(430.79), respectively. Method comparison between the Atellica IM TnIH Assay and ADVIA Centaur® High-Sensitivity Troponin I (TnIH) assay showed a regression slope of 1.045 (95%CI 1.03 to 1.06), intercept of -2.396 pg/ml(95%CI -2.62 to -2.00) (n=77). Serial measurement results demonstrated 100% total agreement for subjects falling above and below the respective assay 95% percentile value, when comparing Atellica IM TnIH Assay with ADVIA Centaur TnIH assay.

Conclusion: The Atellica IM TnIH Assay has demonstrated good precision for detecting low cardiac troponin I concentrations, good correlation and agreement with the Siemens ADVIA Centaur TnIH assay.

A-074

Assessment of Plasma Hepcidin Concentration as a Novel Biomarkers of Acute Coronary Syndrome Severity

Y. Wahed, T. El-Abaseri, A. El-Hawary, E. Ismail. Suez Canal University, Ismailia, Egypt

Background: Hepcidin, produced mainly by liver hepatocytes, is the principal systemic iron regulator. Hepcidin is an acute phase reactant that plays a role in the progression of inflammatory caused diseases including thrombosis formation in coronary artery diseases (CAD). We assessed serum hepcidin level in CAD patients with acute coronary syndrome (ACS). The association of classical atherosclerotic markers such as cardiac troponin I (cTnI), and C reactive protein (CRP) was compared to hepcidin and ferritin serum levels.

Methods: A total of 80 subjects (60 ACS patients and 20 controls) were enrolled.

Results: ACS patients were 68.8% males and 31.3% females. Their overall mean age was 56.00±8.73. Healthy controls mean age was 50.2±9.03 and included 13/65% males and 7/ 35% females. 53.1% of ACS patients were hypertensive and 39.1% were diabetics compared to 15% hypertensive and 10% diabetics in the healthy control group. ACS patients have higher TG, LDL and lower HDL (means114.3±47.6, 127.0±45.2, 35.8±9.3 mg/dl respectively) compared to controls. Mean random blood glucose was 174.4 ±68.2 in ACS and 111.3±30.0 in control subjects. While hepatic iron concentration was 95.3±20.2 μg/g in ACS and 90.3±7.3 μg/g in control subjects, liver iron concentration was 18.0±5.4 μg/g in ACS and 17.0±4.5 μg/g in control subjects.

Conclusion: Hepcidin level in CAD patients with acute coronary syndrome (ACS). The association of classical atherosclerotic markers such as cardiac troponin I (cTnI), and C reactive protein (CRP) was compared to hepcidin and ferritin serum levels. We concluded that serum hepcidin is increased in STEMI compared to the healthy controls. Serum hepcidin and ferritin are elevated using enzyme-linked immunosorbent assay (ELISA). CRP, cTnI, and lipids were measured using spectrophotometry. The results were statistically compared.

A-075

Performance of Emergency Testing Functionalities for Atellica® IM TnIH, hCG and BNP Assays on the Atellica® Solution

M. Sanz de Pedro, J. Diaz-Garzón, J. Iturzaeta Sanchez, P. Fernandez Calle, R. Gomez Rojia, P. Oliver Saez, A. Bano Soto. HOSPITAL UNIVERSITARIO LA PAZ, MADRID, Spain

Background: The objective of this study was to verify the STAT capabilities of the Atellica® Solution, consisting of an Atellica® Sample Handler and two Atellica® IM 1600 Analyzers, with two metrics: (1) turnaround time (TAT) for emergency STAT tests while simultaneously performing routine testing and (2) impact of the STAT capabilities of the system on the TAT of the emergency samples.

Methods: The study reproduced a typical 3 hour peak period of the day for 650 routine samples with 1561 test requests representative of the lab’s workload. To include STAT testing, normally done in a dedicated laboratory, we added to the worklist a representative day’s quantity of High-Sensitivity troponin I (TnIH), total hCG (hCG), and B-type natriuretic peptide (BNP) STAT tests corresponding to those same 3 hours, thus creating a single worklist including both routine and STAT. Hence, we were able to load STAT samples into the recreated peak routine testing and observe TAT from tube scanning on the Atellica Solution to result delivery. Routine samples were loaded in 10 minute intervals; STAT tubes were loaded according to the timestamps collected from the original STAT laboratory data. Since hCG was run both as routine and STAT we were able to measure the impact of the system’s STAT functionalities on TAT.

Results: TAT of STAT assays:

<table>
<thead>
<tr>
<th>Assay</th>
<th>As STAT</th>
<th>As routine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample</td>
<td>Mean TAT (min)</td>
<td>TAT CV (%)</td>
</tr>
<tr>
<td>TnIH</td>
<td>13</td>
<td>10.9</td>
</tr>
<tr>
<td>hCG</td>
<td>6</td>
<td>10.9</td>
</tr>
<tr>
<td>BNP</td>
<td>7</td>
<td>11.1</td>
</tr>
</tbody>
</table>

N/A: Not applicable

Conclusion: The Atellica Solution is able to deliver results with a quick and predictable TAT for STAT assays, including TnIH, hCG, and BNP, while simultaneously performing routine testing with minimal impact on throughput. Furthermore, comparing TAT of hCG in STAT vs. routine shows that the Atellica Solution’s STAT capability effectively reduces TAT and variability.

* Siemens Healthineers supported the study by providing systems, reagents, protocols and contributed to data analysis.

A-076

High-Sensitivity Cardiac Troponin I Whole Blood and Plasma Specimen Comparisons Measured by the ET Healthcare Pylon Point of Care Assay

I. L. Gunislaus, B. Lindgren, J. Nicholson, A. Sexter, K. Schulz, F. S. Apple. Hennepin County Medical Center, Minneapolis, MN

Introduction: Cardiac troponin (cTn) testing is the guideline recommended biomarker for ruling in and ruling out acute myocardial infarction (MI) and risk stratification of patients presenting to emergency departments with ischemic symptoms. High sensitivity (hs) cTn assays are transitioning to become the optimal methods because of improved analytical performance. The objectives of our study were to compare a) POCT hs-cTn concentrations between matched whole blood and plasma specimens from 40 patients admitted through the emergency department using a novel point of care (POC) assay and b) plasma POCT hs-cTn concentrations with plasma measured on central laboratory hs-cTn and Gen 5 cTn assays.

Methods: Fresh, whole blood EDTA anticoagulated specimens (n=40) were collected in the emergency department. Within 2 hours, the whole blood specimens were analyzed, and then immediately centrifuged to separate the EDTA plasma, which were then immediately analyzed. Whole blood and plasma measurements were performed on the novel Pylon hs-cTn assay by ET Healthcare; currently only cleared for patient use in China. Further, the POC Pylon plasma results were compared with a research investigation hs-cTn assay by Abbott (ARCHITECT i1000) and the Roche Gen 5 cTn assay (cobas e601). Specimens were enrolled over a 5-day period. Results: 98% of whole blood and 100% of plasma specimens were measurable
by the Pylon; ranges: whole blood 1.1-6.1 ng/L; plasma 1.4 to 59, ng/L. The correlation between whole blood and plasma showed the following: WB hs-cTnI = 0.98 plasma hs-cTnI + 1.01. The plasma correlations measured on the Pylon and the a) ARCHITECT and b) cobas e601 showed the following: Pylon hs-cTnI = 0.32 ARCHITECT hs-cTnI + 7.85; Pylon hs-cTnI = 0.10 cobas hs-cTnI + 11.05; respectively. The plasma correlation between the ARCHITECT and cobas e601 showed the following: ARCHITECT hs-cTnI = 0.26 cobas hs-cTnI + 11.56.

Conclusions: Preliminary findings of the ROC Pylon ET Healthcare hs-cTn assay showed excellent agreement between whole blood and plasma. Correlation between the Pylon hs-cTnI and ARCHITECT hs-cTnI assays was excellent for 36 of the 40 plasma samples studied; 4 samples showed higher results on the Pylon than the ARCHITECT, resulting in a decrease in the overall correlation. Correlation of cobas hs-cTnI with both the Pylon and the ARCHITECT was poor. Additional studies are underway to evaluate the clinical performance of this ROC hs-cTnI assay.

A-077

Method Comparison of 5th Generation “High-Sensitivity” Troponin T with 4th Generation Troponin T

N. J. Werts, R. Engineer, A. J. McShane. Cleveland Clinic, Cleveland, OH

Background: The Food and Drug Administration cleared Roche Diagnostics Elecsys Troponin T Gen 5 STAT (gen5 cTnT) assay in January 2017, making it the first next generation troponin assay available in the United States. The assay was implemented at our hospital to assist with the rapid rule out of acute myocardial infarction (AMI) and risk stratification of acute coronary syndromes. Analytical relationships were explored between gen5 cTnT and Troponin T STAT (gen4 cTnT; Roche Diagnostics), with emphasis near lower limits of measure. Further, the association between plasma creatinine concentration and gen5 cTnT result was evaluated.

Methods: Comparisons were made between the gen5 cTnT and gen4 cTnT assays on 4 Cobas 8000 e602 (Roche Diagnostics) instruments. All non-less than gen4 cTnT (>0.09 ng/mL) and gen5 cTnT (>5 ng/L) results were plotted, and Deming regression analysis was performed. Further, additional comparisons were made between plasma creatinine concentration and gen5 cTnT. Gen5 cTnT results >51 ng/L were excluded from analysis and <6 ng/L results were included as 6 ng/L. The comparisons were made between the averaged gen5 cTnT result per group and the grouped plasma creatinine concentration: 0.60-0.79, 0.80-0.99, 1.00-1.19, 1.20-1.39, 1.40-1.59, 1.60-1.79, and 1.80-1.99 ng/dL. Data for all studies was collected from 07/05/17 to 12/03/18.

Results: The analysis included 614 points from a gen5 cTnT (y axis) range of 6 to 1391 ng/L and a gen4 cTnT (x axis) range of 0.010 to 1.360 ng/mL. The regression analysis displayed a Pearson coefficient (R) of 0.9845, a slope of 901, and intercept of 24. Deming regression analysis was also performed in a smaller sub range, focused on the lower measuring range (i.e. closer to clinically important thresholds). The analysis plotted 373 points from a gen5 cTnT (y axis) range of 6 to 82 ng/L against a gen4 cTnT (x axis) range of 0.010 to 0.050 ng/L. The regression analysis displayed an R of 0.7806, a slope of 1490, and an intercept of 11. The sub range displays a lower correlation between whole blood and plasma showed the following: WB hs-cTnI = 0.7806, a slope of 1490, and an intercept of 11. The sub range displays a lower correlation compared to the larger range and a proportional bias. To further evaluate the differences in the methods, gen4 cTnT results <0.010 ng/mL were compared to the corresponding creatinine concentration group, displaying an R of 0.987. The lowest plasma creatinine concentration group (0.60-0.79 mg/dL) yielded an average gen5 cTnT of 9 ng/L, and the highest plasma creatinine concentration group (1.80-1.99 mg/dL) gave an average gen5 cTnT of 27 ng/L. Conclusion: Overall, gen5 cTnT has a strong linear relationship versus its predecessor assay, gen4 cTnT. However, the correlation decreases towards their respective lower limits. Gen5 cTnT also displays a strong relationship to plasma creatinine concentration.

A-078

NT-proBNP assays that are based on antibodies which are specific to nonglycosylated regions of NT-proBNP display a similar diagnostic accuracy in distinguishing heart failure patients compared to the Roche NT-proBNP assay

A. G. Semenov1, E. E. Feygina1, K. R. Sfeirian1, N. N. Tamm2, M. N. Bloshchitsyna2, A. B. Postnikov2, A. G. Katrukha1, 1HyTest Ltd., Turku, Finland, 2School of Biology, Moscow State University, Moscow, Russian Federation

Background: N-terminal fragment of pro-B-type natriuretic peptide (NT-proBNP) is a useful blood biomarker for the diagnosis of heart failure (HF). NT-proBNP assay is O-glycosylated within the central part and present in the circulation as a pool of molecules with different glycosylation levels. An automated NT-proBNP immunoassay manufactured by Roche is widely used for NT-proBNP measurements. This assay employs monoclonal antibodies (mAbs) that are specific to the epitopes 27-31 and 42-46 in the central region of NT-proBNP. One of the mAbs is specific to the partially glycosylated region of NT-proBNP as the epitope 42-46 comprises Ser42, which is modified by glycosidic residues. The presence of O-glycans at this site makes NT-proBNP undetectable by the Roche NT-proBNP assay due to the steric hindrance. In light of this, the assay is able to detect only the NT-proBNP fraction that is nonglycosylated at the 42-46 region and not the "total" NT-proBNP, i.e. both glycosylated and nonglycosylated subfractions. Since O-glycosylation tends to be heterogeneous, its pattern and extent might vary significantly among individuals and this could in turn impact the clinical value of NT-proBNP measurements by glycosylation-sensitive NT-proBNP assays.

We have developed an alternative type of NT-proBNP immunoassays that are not affected by analyte glycosylation and are able to measure the concentration of the “total” NT-proBNP. The aim of this study was to compare the diagnostic accuracy of measurements of the “total” NT-proBNP (by two prototype immunnoassays) with measurements of NT-proBNP that is nonglycosylated at Ser42, subtraction of NT-proBNP (by the Roche NT-proBNP assay) in distinguishing HF from non-HF patients.

Methods: NT-proBNP levels were measured by two HyTest’s prototype NT-proBNP assays (capture mAb - detection mAb: 29D12 - NT34, 15C4 - 13G12, and) and the Roche NT-proBNP assay (automated Roche Cobas e 411 analyzer) in EDTA-plasma samples that were obtained from 51 patients who had been diagnosed with HF and 53 healthy individuals (age-matched). HyTest’s prototype NT-proBNP assays were linear in the range of 20 to 80,000 ng/L and the detection limits were 5-10 ng/L. Recombinant nonglycosylated NT-proBNP 1-76 (HyTest, produced in E. coli) was used as a calibrator in the prototype NT-proBNP assays. The diagnostic accuracy of the assays was analyzed by the comparison of the ROC curves.

Results: ROC-AUC for the prototype assays 29D12 - NT34 = 0.951/0.946; specificity 0.86/0.84 and specificity 0.93/0.98 respectively) compared to 0.965 (specificity 0.86 and specificity 0.98) for the Roche NT-proBNP assay. Differences were statistically insignificant (p-value = 0.365/0.369).

Conclusion: NT-proBNP immunoassays that are based on antibodies which are specific to nonglycosylated regions of the NT-proBNP molecule are expected to have at least a similar clinical value for HF diagnosis as the Roche NT-proBNP assay that detects only a subfraction of endogenous NT-proBNP. Taking into account the known high variability in levels and site occupancy of O-glycosylated proteins, we suggest that immunoassays which measure “total” NT-proBNP levels might be advantageous for HF diagnostics and/or therapy monitoring in certain groups of patients and disease states due to their ability to detect endogenous NT-proBNP independently of its glycosylation status.

A-079

Do High-Sensitivity Cardiac Troponin T Clinical Performance Data in Package Inserts Reflect Realistic Clinical Expectations?

R. H. Christenson1, S. Dub1, F. S. Apple2, R. M. Nowak1, J. McCord1, C. R. dcFilippi1. 1Univ of Maryland School of Medicine, Baltimore, MD, 2Hennepin County Medical Center and University of Minnesota Minneapolis, MN, 3Henry Ford Health System, Detroit, MI, 4Henry Ford Hospital, Detroit, MI, 5Inova Heart and Vascular Institute, Falls Church, VA

Background: Cardiac troponin (cTn) is a cornerstone for diagnosis and management of myocardial infarction (MI). High-sensitivity troponin (hs-tn) provides earlier MI rule-in/rule-out. The 2015 European Society of Cardiology guidelines proposed hs-Tn algorithms for NSTEMI-management. However, estimates of hs-cTn performance may vary based on the anchor-time used for analysis. Typically cTn data have been organized relative to the “first study sample” (1stSS) collection time, including in
Cardiac Markers

manufacturers’ package inserts. Alternatively data can be organized based on time of presentation (TOP). We investigated diagnostic performance of the ADVIA Centaur® hs-TnI (TNIH) up to 3.5 hours using TOP or 1stSS anchor-time.

**Methods:** Samples from >2,300 ‘all-comer’ suspected MI patients were collected at 29 IRB-approved sites; 310 (13%) patients were adjudicated MI positive. The TNIH assay was validated as hs-TnI: total CV was 2.9% at the female 99th percentile (37 ng/L) using the AACC Universal Sample bank, 58.9% and 85.3% of values from healthy women and men, respectively, exceeded LoD (1.6ng/L).

**Results:** Median delay between local standard-of-care first blood draw and 1SS was 49 min. Table-Section A shows TNIH sex-specific performance based on TOP analysis (n=4,502 observations). Table-Section B displays sex-specific performance using 1SS (n=6,346 observations). At 3.5-hours, TOP sensitivity was 95.8% & 89.7% and Negative Predictive Value (NPV) was 99.5% & 98.1% for women and men, respectively. For 1SS at 3.5-hours, sensitivity was 95.0% & 89.2% and NPV was 99.3% & 97.6% for women and men, respectively. Although at 3.5-hours, TOP (n=198) had more adjudicated MIs than 1SS (n=114) (p<0.001), sensitivity/NPV was not significantly different than anchoring at 1SS (p-value=0.44).

**Conclusion:** Reporting performance relative to TOP or the 1SS does not yield different values for sensitivity/NPV or other MI diagnostic parameters at 3.5 hours. We advocate reporting data anchored to clinical presentation time to facilitate harmonizing with clinical guidelines.

### A-080

**Macroprotonin T causing a false positive troponin elevation**

P. O. Collinson, M. Mbedu, C. Hunt. **St George’s Hospital, London, United Kingdom**

Presentation: A 54 year old Asian British male was admitted with a 4 day history of chest pain for 7 days. Past medical history: Chronic hepatitis B (e-Antigen negative), non-alcoholic steatohepatitis, hypertension and type-2 diabetes. Past medical history for chest pain 4 and 2 years prior to this episode. Family history: Type 2 diabetes, hypertension and hypercholesterolaemia.

Clinical course: Troponin T (cTnT) Roche Diagnostics Casbas 8000 (10% CV = 13ag/L, 99th percentile URL = 14ng/L) was elevated on admission and noted to remain consistently elevated. Investigations: Imaging by thoracic CT (aortic imaging, no abnormality detected), coronary angiography (no obstructive epicardial disease) and cardiac MRI (no evidence of injury or wall motion abnormality) did not support acute myocardial injury as a cause for the raised troponin. An analytical interference was suspected and serial dilution and polyethylene glycol (PEG) precipitation of the sample was performed and the sample was analysed for cardiac troponin I (Abbott diagnostics hs Tnl, 10% CV = 4.7 ng/L, 99th percentile URL = 26.2 ng/L). Results: cTnT was <2ng/L. Serial dilution showed comparable recovery with a known native high troponin sample (y=0.086x - 60.759, R² = 0.9986). PEG precipitation showed a large disparity in recovery between original measurements and against known native troponin samples (Day 4 = 1.13% and Day 5= 1.36% recovery, control samples = 94.46% and 85.09% recovery). Conclusion: The results were consistent with macroprotonin and not acute cardiac injury. Macroprotonin T has not been widely reported.

<table>
<thead>
<tr>
<th>Date</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troponin T (ng/L)</td>
<td>1588</td>
<td>1842</td>
<td>1690</td>
<td>1739</td>
<td>1684</td>
<td>1718</td>
</tr>
</tbody>
</table>

### A-082

**Natriuretic Peptide NT-proBNP: Method comparison of two analysers**


**Background:** Here we summarize the outcome of a comparison study to evaluate NT-proBNP assay. It has been performed at two analysers, AQT90 Flex from Radiometer®, a point of care technology, and cobas e801 from Roche Diagnostics®, the gold standard.Natriuretic peptides are secreted by the heart into the bloodstream as a result of an increase of intracardiac volumes and pressures. NT-proBNP has become an important biomarker of heart failure. The aim of the study is to compare the results and their interchangeability in order to determine the concordance between both immunoassays. **Methods:** The measurements were performed in serum samples from random real patients. The samples were processed in both analysers at the same day, in parallel. Statistical analysis was carried out with the MedCalc software, where the
correlation was calculated by the Pearson’s coefficient, the Passing-bablok regression and Bland Altman plots. Results: Below, is a summary data table of the regression results.

<table>
<thead>
<tr>
<th>Test</th>
<th>Instrument</th>
<th>Study Unit</th>
<th>N</th>
<th>Correlation coefficient Pearson r</th>
<th>Passing-Bablok Slope</th>
<th>Intercept</th>
<th>Deviation from linearity</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT-proBNP</td>
<td>AQTP0 Flex; Cobas e801</td>
<td>pg/mL</td>
<td>124</td>
<td>0.9974</td>
<td>0.953</td>
<td>0.9963</td>
<td>0.9982</td>
<td>0.051</td>
</tr>
</tbody>
</table>

Results show a high degree of correlation coefficient and adjustment to linearity; however, there exists a proportional bias. It would be necessary to check the clinical concordance of the results, checking if this bias could be ignored under our working standard conditions. Concordance according to cut-off for heart failure was 96% (119/124). These five different results were in grey zone, very close to cut-off. Conclusion: Results from both analysers show a good correlation between the two methods. Due to the high clinical concordance, the proportional bias we found in the method comparison could be ignored and the interchangeability of methods is possible. Point of care technology offers a short response time what added to a good correlation results with the gold standard open an option to further accelerate the diagnosis of heart failure and thereby the initiation of adequate therapy.

A-083

Development and Evaluation of Analytical Performance of Immunomassay for the High Sensitive Measurement of Cardiac Troponin I for LUMIPULSE® L2400 Analyzer

T. Tokunaga, Y. Kawada, S. Yamauchi, S. Kojima, K. Moriyama, K. Aoyagi. Fujirebio Inc, Tokyo, Japan

Background: Cardiac Troponin I (cTnI) and T (cTnT) are being used internationally as the standard biomarkers for the detection of myocardial injury, risk stratification in patients suspected of acute coronary syndrome (ACS) and for the diagnosis of myocardial infarction. In the recent international guidelines, algorithms are presented for rule-in and rule-out of non-ST-elevation myocardial infarction with the use of high-sensitivity (hs) cTnI or cTnT. We have developed new high sensitivity cTnI iVD kit, Lumipulse Presto hs Troponin I which is a fully automated chemiluminescence enzyme immunoassay (CLEIA) for LUMIPULSE L2400 analyzer. The higher throughput put (240 tests/h) and STAT mode (approx. 15 minutes measurement time) of LUMIPULSE L2400 allows for quicker diagnosis. The analytical performance of the Lumipulse Presto hs Troponin I assay was evaluated, and compared with other hs cTn assay.

Methods: Lumipulse Presto hs Troponin I is a two-step sandwich CLEIA. The resulting reaction signals are proportional to the amount of cTnI in the serum or plasma sample allowing quantitative determination of cTnI. Analytical performance of the assay was evaluated on LUMIPULSE L2400 analyzer (with STAT mode) according CLSI guidelines.

Results: Limit of blank (LoB), detection (LoD) and quantitation (LoQ) were 0.5 pg/mL, 0.9 pg/mL and 2.7 pg/mL or less, respectively. The 99th percentile URL, imprecision at 99th percentile and detectable healthy population were estimated to be 21.0 pg/mL, 1.7%CV and 93%. Linearity was demonstrated over the range 2.5 to 46151.5 pg/mL. The coefficient of variation (CV) of total imprecision was 1.3 to 4.2%CV with 8 levels of samples. Results of method comparisons were correlation coefficient r = 1.00, regression slope = 1.07 against Lumipulse G hs Troponin I, correlation coefficient r = 1.00, regression slope = 0.98 against Architect high sensitivity Troponin I. While correlation with Roche hs Troponin T was correlation coefficient r = 0.93, regression slope = 10.13. The measurement value variations by various interferences (bilirubin, hemoglobin, triglycerides, chyle, total protein, rheumatoid factor and HAMA) were ≤ 10% at the clinically high enough concentrations. The assay showed high precision, high robustness and high correlation with current hs-cTn assays, Lumipulse G hs Troponin I and Architect high sensitivity Troponin I assays. It is expected that the new assay is useful as an aid in the diagnostics and risk management of ACS patients.

A-084

Human Epididymis protein 4 levels in acute cardiac failure

c. o. mina, c. castillo perez, b. torrubia dodero, l. rodriguez alonso, m. cebrian ballesteros. HU.Fundacion Jimenez Diaz, madrid, Spain

Introduction: Cardiac failure is a major health problem worldwide that concerns the health systems of developing countries. Cardiac failure is a clinical diagnosis based in specific signs and symptoms but several laboratory markers had been proposed for its diagnosis. NT-proBNP is the only biomarker used for the diagnostic and prognostic of cardiac failure and it had been included in specific guidelines. There are a few studies that have seen association between HE4 (human epididymis protein 4) and acute heart failure severity in patients without tumoral pathology and normal renal function.

Objective: We evaluated the level of human epididymis protein 4 (HE4)in selected patients with normal renal function, without gynecological pathology and non tumoral pathology described in the clinical histories.

Methods: 22 patients that consulted the Emergency Department, with myocardial infarction were selected. Determination of NT-proBNP was made in the first 24 hours seeking for a laboratory diagnostic of heart failure. The determination of NT-proBNP and HE4 was made using an immunologic assay. To analyze the data we have used SPSS 16. Patients were divided in two groups using the NT-proBNP diagnostic value as recommended by the European Society of Cardiology with 88% positive predicting value: 1. Heart failure group (HFG); 13 patients (6 men and 7 women). 2. non Heart failure group (nHFG). 9 patients (4 men and 5 women)

We calculated the medians and the IQR of both groups and the area under the curve (AUC), sensitivity and specificity were estimated.

Results: The mean age of HFG group was 62.22 and for the nHFG group was 70.25. No sex or age differences were observed. The HE4 median and IQR of HFG group and nHFG group was 185.44 (98.96) pmol/L and 59.30 (7.84) pmol/L respectively. We found statistically significant differences between both group (p=0.002). The AUC was 0.88 [ IQR95% = (0.71-1.00) ] with 75% sensitivity and 100% specificity with a cutoff point of 97.1 pmol/L.

Conclusions: The present study suggests a positive association between increased HE4 levels in acute cardiac failure. Further studies are needed to investigate the value of HE4 as a biomarker in acute heart failure.

A-085

Analytical performance of the Elecsys® Troponin T Gen 5 STAT assay

R. L. Fitzgerald1, J. E. Holland2, W. S. Peacock1, A. T. Limkakeng3, N. Breitenbeck4, E. J. Rivers5, C. Dinkel-Keuthage6, C. deFilippis7, JU. CSD, San Diego, CA, 1Thomas Jefferson University, Philadelphia, PA, 2Bayor College of Medicine, Houston, TX, 3Duke University, Durham, NC, 4NB Research Inc, Indianapolis, IN, 5Roche Diagnostics, Indianapolis, IN, 6Roche Diagnostics, Penzberg, Germany, 7Inova Heart and Vascular Institute, Falls Church, VA

Background: The Elecsys® Troponin T Gen 5 Short Turn Around Time (TnT Gen 5 STAT; Roche Diagnostics) assay received FDA clearance in January 2017 and provides a high-negative predictive value for ruling out acute myocardial infarction. We report analytical performance of this assay, including specificity versus diverse troponin isoforms.

Methods: Precision was evaluated using human Li-heparin plasma and PreciControl Troponin samples per Clinical and Laboratory Standards Institute EP05-A2; two runs per day in duplicate for 21 days (n=84). Samples were measured using the Elecsys TnT Gen 5 STAT assay on the cobas e 411 and cobas e 601 analyzers (three reagents lots). Specificity for cardiac troponin T (at concentrations of 14ng/L, 4,000ng/L and 7,000ng/L) was tested versus skeletal muscle troponin T and I, cardiac troponin I, and human troponin C. Cross-reactivity with endogenous substances (including biotin) and commonly used cardiac-specific drugs was tested at cardiac troponin T concentrations of 15ng/L and 9,000ng/L. Analytical specificity criteria were: recovery within ±14ng/L for cardiac troponin T concentrations <14ng/L; recovery within ±10% for cardiac troponin T concentrations ≥14ng/L.

Results: On the cobas e 601 analyzer, coefficient of variation (CV) ranges for repeatability and intermediate precision were 0.7-3.0% and 1.5-6.4%, respec.
Cardiac Markers

A-086 Heart-type fatty acid-binding protein measurements to aid in interpreting abnormal and non-changing cardiac troponin concentrations

L. LIVICA, C. AINSWORTH, D. M. ARNDT, T. SCOTT, L. CLARK, K. MACKETT, R. WHITLOCK, A. WORSTER, P.A. KA VSAK, McMaster University, Hamilton, ON, Canada, McMaster University and Hamilton Health Sciences, Hamilton, ON, Canada, Hamilton Health Sciences, Hamilton, ON, Canada

Background: Stable or non-changing abnormal high-sensitivity cardiac troponin (hs-cTn) concentrations may indicate the presence of cardiac diseases other than acute coronary syndrome, or might even identify an analytical interference resulting in this high concentration. There are heterophile antibodies, autoimmune antibodies to cardiac troponin, and even macrocomplexes that may result in an abnormal hs-cTn concentration. When evaluating possible interferences affecting hs-cTn assays it may be useful to measure another cardiac biomarker using another type of methodology. In this regard, heart-type fatty acid binding protein (H-FABP), a biomarker that is released early after cardiac injury, and can be measured turbidimetrically on chemistry analyzers with open-channel capabilities might prove to be useful when investigating a possible analytical reason for abnormally high and non-changing hs-cTn concentrations. Our objective was to validate the Random H-FABP on the Abbott ARCHITECT c8000 platform, with total imprecision, linearity, and comparability between different materials.

Methods: The Random H-FABP assay, a latex particle-enhanced turbidimetric assay, was loaded on the Abbott ARCHITECT c8000 platform, with total imprecision at two concentrations assessed over 2 months, linearity evaluated (5 different concentrations), stability (freeze [-80°C]/thaw cycles and room temperature with EDTA plasma) assessed, with matrix comparison (lithium heparin versus EDTA plasma) and correlation with Abbott hs-cTn concentrations in EDTA plasma. Also, EDTA plasma samples from patients with persistently elevated and stable cTn concentrations (Abbott hs-cTn≥52ng/L which equates to ≥2xULN 99th-26ng/L with change between results <20%) from patients with a primary discharge diagnosis not related to a cardiac etiology were collected and frozen (-20°C). These samples were tested with the H-FABP assay (ULN 99th-6.3ng/L) and with polyethylene glycol (PEG) precipitation to identify macrocomplexes. Results: The imprecision (%CV) with Random QC level 1 = 5.39 ug/L was 14.8% (n=40) and QC level 2 = 31.16 ug/L was 3.6% (n=37). The assay was linear from 3.8 ug/L to 95 ug/L. H-FABP was stable after 4 freeze/thaw cycles and, at room temperature, up to 150 hours in EDTA plasma as differences from baseline measurements (i.e., room temperature sample H-FABP = 12.50 ug/L and freeze/thaw sample H-FABP = 15.11 ug/L) were <20%. Comparison between lithium heparin and EDTA plasma samples for H-FABP was acceptable (mean bias=0.05ug/L, n=20 paired samples, with H-FABP range from 4.94 to 25.76 ug/L). The correlation between H-FABP and hs-cTn results from 100 EDTA plasma samples was weak to moderate (Spearman’s rho = 0.383 (95%CI: 0.201 to 0.539); p<0.001. During the validation, there were 4 patients with a non-cardiac discharge diagnosis with elevated and stable hs-cTn concentrations ≥2xULN, all had H-FABP concentrations ≥2xULN with 3 patients also having macrocomplexes that resulted in the high hs-cTn concentration. Conclusion: The Random H-FABP assay on the Abbott ARCHITECT c8000 analyzer yielded acceptable imprecision, linearity, and comparability between different materials and under different storage conditions. H-FABP measurement might be useful when investigating patients with persistently high hs-cTn concentrations who do not have a clear cardiac etiology for this elevation; as the presence of macrocomplexes might be the cause for the elevation.

A-087 Characterisation of microparticles in patients with acute coronary syndrome - a pilot study

B. Gospodinov 1, L. Wissgrill 1, P. Haller 1, U. Bürgi 1, P. Schüssli 1, M. Batscharof 1, A. Vuillomiennet 1, R. Ennser 1, A. R. Huber 1, K. Huber 1, M. Hämmerer-Lercher 1, A. Spitteler 2, 1Institute for Laboratory Medicine, Kantonsspital Aarau AG, Aarau, Switzerland, 2Division of Neonatology, Pediatric Intensive Care and Neuropediatrics, Medical University of Innsbruck, Vienna, Austria, 3rd Department of Medicine, Cardiology and Intensiv medicine, Medical University of Innsbruck, Batschwaroff Center for Cardiovascular Research, Vienna, Austria, 4BL Centre for Emergency Medicine, Kantonsspital Aarau AG, Aarau, Switzerland, 5Department for Cardiology, Kantonsspital Aarau AG, Aarau, Switzerland, 6Department for Operative Intensive Care Medicine, Kantonsspital Aarau AG, Aarau, Switzerland

Background: Extracellular vesicles (EVs) in human blood can be subdivided into microparticles (MPs), 0.1-1µm in size, and exosomes below 0.1µm in size. MPs consist of a phospholipid bilayer and a substantial number expose procoagulogenic phosphatidylyserine. They derive from different cell types upon proliferation, activation or apoptosis. It was shown that the number of MPs increases in thrombotic, inflammatory and hypoxic situations and it is suggested that they play an important pathophysiological role. We evaluated the amount and subtypes of MPs in patients with acute coronary syndrome (ACS) compared to a control group of patients presenting with chest pain, but without ACS. The characterization of MPs in ACS may give a better insight into the pathophysiology of the disease and add prognostic relevant information for the risk stratification.

Methods: This is an ongoing study that recruited patients with thoracic pain suggestive for ACS from the emergency unit of the Kantonsspital Aarau/Switzerland and from the University Hospital in Vienna/Austria. Patients with recent myocardial infarction, malignancy, pulmonal embolism, pneumonia, sepsis or acute infection, severe heart or renal failure were excluded as in these patients increased MPs are suspected. Preliminary results derive from the first center, where patients have been divided into ACS-positive (n=26) and ACS-negative (n=36) groups are presented here. Citrate blood was immediately drawn upon presentation (t1), and for ACS-patients also approx. 4 hours later (t2) and on the next day (t3). Blood tubes were transported to the laboratory on foot without agitation and immediately centrifuged twice to remove platelet free plasma (FFP). FFP was stored at -80°C until batch analysis using a 4 laser flow cytometer (CytoFLEX, Beckman Coulter). The gate for MPs was set with silica beads and triggering was done on Annexin-V Cy5. Different MPs were investigated using cellcalc and Annexin-V in combination with fluorescence labeled antibodies against erythrocyte (EMAs), platelet (PMPs), monocyte (MPMs) and endothelium (EnMPs) derived MPs. Additionally, CRP and N-terminal pro B-type natriuretic peptide (NT-proBNP; both on a Dimension Vista from Siemens Healthineers) and high-sensitivity cardiac troponin I (hs-cTnI; Architect analyser from Abbott Diagnostics) were measured. Mann-Whitney U test for between group comparison, Wilcoxon test for within group comparison and Spearman rank correlations were performed by SPSS 24.

Results: These preliminary results show that Annexin-V positive MP levels were significantly increased in ACS-patients at t2 and t3 compared to controls (p=0.008 and p=0.038, respectively) and between ACS patients at t1 and t2 (p=0.039). EnMP concentrations (CD31+CD44+CD146+CD42+) were significantly higher in ACS-patients than in controls upon collection (p=0.03) and significantly higher at t2 in ACS compared to controls. Simultaneous serum CRP levels showed that for the subgroup of NSTEMI patients. There was a significant correlation between EnMPs and CRP (r=0.388, p<0.002), hs-cTnI (r=0.408, p=0.002) and NT-proBNP (r=0.486, p<0.001).

Conclusion: Annexin-V positive MPs and EnMPs were significantly increased in ACS patients compared to controls. Further, EnMP concentrations correlated significantly with established cardiac markers, suggesting Annexin-V and EnMP as prospec-
Performance Evaluation of Atellica IM High-Sensitivity Troponin I Assay in a CORE Laboratory

B. Gonzalez de la Presa, X. Filella, N. Rico, L. Macias, C. Domingo, A. Mira, J. Bedini. Hospital Clinic Barcelona, Barcelona, Spain

Background: The objective of this study was to verify the analytical performance (precision) of the Siemens Healthineers Atellica IM High-Sensitivity Troponin I (TnIH) assay and ADVIA Centaur and Beckman Coulter ARCHITECT high-sensitivity Troponin I (TnIH) assays. Methods: The assay is a dual-capture sandwich immunoassay using magnetic latex particles, a proprietary avidin system, and three monoclonal antibodies. Precision studies were performed according to CLSI protocols EP03-A3 and EP15-A3 using lithium heparin plasma samples - two sample pools (SP), and three levels of controls. One aliquot of each sample pool and each QC material was tested in duplicate in two runs per day on each analyzer for a minimum of ten days with one lot of reagent and calibrator. Each run was separated by at least a two hour time interval. A total minimum of 40 replicates were generated per sample. Hemolyzed samples (150 mg/dL and 500 mg/dL) and samples spiked with biotin (30 and 1500 mg/dL) were run in duplicate on the Atellica IM TnIH assay.

Results: Precision studies agreed with the manufacturer’s claims: Within day (repeatability) CV(%) were 3.0 (3.6), 2.7 (2.6), 1.7 (1.6), 2.2 (2.6), and 1.5 (1.6) for concentrations of 11.43 (SP), 25.57 (SP), 98.48, 259.22, and 8505.88 ng/L; within lab (total) CV(%) were 5.8 (6.0), 4.5 (5.1), 2.6 (2.7), and 1.5 (1.8) respectively. Method comparison of Atellica IM TnIH assay vs. ADVIA Centaur TnIH assay showed a regression slope of 0.88 (95%CI 0.862 to 0.902), intercept of 0.77 (95%CI 0.33 to 2.61), and correlation coefficient r=0.997 (n=39); and, Atellica IM TnIH assay vs. Dimension EXL TnIH assay showed a regression slope of 0.97 (95%CI 0.933 to 1.014), intercept of 0.13 (95%CI -0.63 to 0.90), and correlation coefficient r=0.998 (n=99). All hemolysis (up to 500 mg/dL) and biotin (up to 1500 mg/L) samples tested with the Atellica IM TnIH assay demonstrated ≤10% change in results. Conclusion: The Atellica IM TnIH assay has demonstrated good precision for detecting low cardiac troponin I concentrations and good correlation with the Dimension EXL TnIH assay and a slight negative bias with the ADVIA Centaur TnIH assay. At levels of biotin up to 1500 mg/mL and hemolysis up to 500 mg/dL, there was ≤10% change in results.

Atellica IM High-Sensitivity Troponin I Assay: Analytical Evaluation Among University Hospitals

K. Peoc’h1, V. Chicha-Cattoir2, Y. Habhabou3, H. Mansour4, T. Robert1, S. Ouaheb1, A. Dauphin1, N. Seta4, G. Leveque1, Paris Diderot University, Paris, France; 1APHP, HUPNYS, Hôpital Bichat, Clichy, France; 2APHP, HUEP, Hôpital Tenon, Paris, France; 3APHP, HUPNYS, Hôpital Bichat, Paris, France; 4APHP, HUPNYS, Hôpital Bicêtre, Paris, France; 5APHP, HUPNYS, Paris, Hôpital Bicêtre, Paris, France

Siemens Healthineers supported the study by providing systems, reagents, and protocols, and contributed to data analysis.

Background: Cardiac troponin is the favored biomarker for aiding in the diagnosis of myocardial infarction (MI). By definition, high sensitivity troponin assays must demonstrate increased analytical sensitivities and gain of precision at the lower concentrations, allowing the time-point shortening of serial measurements, and improving their diagnostic sensitivity for early MI detection. The Atellica® IM High-Sensitivity Troponin I (TnIH) Assay is an in vitro diagnostic immunoassay for the quantitative determination of cardiac troponin I (cTnI) in serum or plasma (lithium heparin). The goal of this study was to check TnIH Assay analytical precision run on Atellica® IM 1600 Analyzer, and to compare TnIH Assay to Abbott ARCHITECT STAT High Sensitive Troponin-I (ARCHI-TECT TnIHs) and ADVIA Centaur High-Sensitivity Troponin I (TNIIH) assays.

Methods: The Atellica IM TnIH Assay is a dual-capture sandwich immunoassay using three monoclonal antibodies, magnetic latex particles and an unique proprietary avidin system for chemiluminescence detection. Precision studies were performed according to CLSI protocols EP05-A3 and EP15-A2 using lithium heparin plasma samples (two sample pools), and three levels of quality controls (QC). One aliquot from each pool and each QC material was tested in duplicate using one lot of reagent and calibrator (two runs per day on each analyzer) during at least ten days. Each run was kept apart by at least a two hour time interval. At least 40 replicates were generated for each of the two sample pools and the three levels of QC. Method comparison was performed according to EP009-A3, cTn samples (lithium heparin) were obtained from acute chest pain patients selected in three university Emergency Departments (Bichat, Beaujon and Tenon). Serial samples were collected on two times, one at admission and one within 1, 2, 3, or up to 6 h later and were tested using the three cTn assays. Assay comparisons were made using Deming correlation.

Results: Within run repeatability for cTn concentrations of 10.7, 25.0, 95.0, 252.8, 5171.0 ng/L (CV(%) were 3.6 (0.38), 2.9 (0.73), 1.6 (1.05), 1.7 (4.35), and 1.2 (6.703). Within lab (total) CV(%) were 8.6 (0.72), 3.4 (0.85), 4.0 (3.78), 4.3 (10.93), 2.7 (154.90), respectively. Atellica IM TnIH Assay comparison with Abbott ARCHITECT TnIHs assay (range 0.28 ng/L to 15,989 ng/L for Atellica IM TnIH Assay and range 0.2 ng to 30.602 ng/L for Abbott ARCHITECT assay; n=99) showed a slope of 1.01 (95%CI 0.885 to 1.152) and intercept of 0.77 (95%CI 0.49 to 1.988), r=0.964, and with ADVIA Centaur TnIH assay (range 0.28 ng to 15.988 ng/L for Atellica IM TnIH assay and range 0.36 ng to 16.473 ng/L for ADVIA Centaur Tn IH assay; n=97) a slope of 1.02 (95%CI 1.004 to 1.039) and intercept of 0.68 (95%CI 0.437 to 1.065), r=0.999.

Conclusion: The Atellica IM TnIH Assay demonstrated acceptable precision for detecting low cTn concentrations and confirmed the manufacturer’s claims. Furthermore, no significant analytical bias was found when compared to two commercially available high sensitivity cTn assays.

Will different clinical cut-offs impact the diagnostic accuracy of hs-cTnI assays in suspected ACS patients?

Suni S1, L. M. Motta2, A. Molteni1, A. Vozzi2, P. Bianchi3, E. Morenghi1, F. Mauri4, B. Barbieri2, D. Biacco5, M. Ciotti2, M. N. Monari2. 1Beckman Coulter, Inc., 250 South Kraemer Boulevard, CA, 2IRCCS: Humanitas clinical and research center; Via manzoni 56, Italy; 3IRCCS: Humanitas clinical and research center; Via manzoni, 56, Italy, 4IRCCS: Humanitas clinical and research center, Via Manzoni, 56, Italy

Background: Chest pain is a common cause of hospital admission world widely and is a major burden on healthcare resources. Cardiac troponin assays have substantially improved the accuracy of diagnosis and prognostic assessment of patients with suspected acute coronary syndrome (ACS). We aim to investigate the influence of different choices of cut-offs for high sensitivity cardiac troponin I (hs-cTnI) assays in patient admission or discharge (according to assigned color code and pain during triage), in order to identify the best scenario in terms of diagnostic accuracy and the need of hospitalization.

Methods: METHODS: A retrospective analysis was conducted on 586 Emergeny Department (ED) patient records within a month who had chest pain complaints in 2017. Only patients who were diagnosed with ACS were included in the analysis. Patients with non-cardiac diagnosis such as thoracic trauma were excluded. All eligible patient samples were measured using Beckman Coulter Access hsTnI and Abbott ARCHITECT hsTnI assays. We investigated three different scenarios using established hs-cTnI cut-off values for ruling in chest pain patients in our population: Beckman Coulter Access hsTnI’s manufacture insert (male 34 ng/L and female 15 ng/L) and Atellica IM TnIH assay (male 19.8 ng/L and female 11.6 ng/L), and 99th percentile cut-off from Abbott hsTnI’s manufacture insert (male 34 ng/L and female 15 ng/L) and 12 ng/L recommended by Dr. Shah’s group for Abbott hsTnI (NCT01852123). Factors that could impact the need of hospitalization were further analyzed.

Results: RESULTS: We included 338 patients (178 men and 160 women) with ACS diagnoses in our final analysis. The need of hospitalization was associated with troponin values above the hs-cTnI cut-offs adopted in each scenario with statistical significance (Abbott, p-value < 0.001; Beckman Coulter, p-value < 0.001; Shah, p-value < 0.001). No statistically significant difference was found among the three scenarios using various hs-cTnI cut-offs in identifying hospitalized patients. Moreover, the higher hsTnI cut-off is associated with an increased probability of admission, corrected for age, gender and color code (Abbott odds ratio (OR) 7.4, 95% CI 2.89-20.75, p<0.001; Beckman 3.93, 95%CI 1.89-8.18, p<0.001; Shah 5.06, 95%CI 2.51-10.22, p=0.002). The hospitalization is highly associated with the color code (p<0.001) given during the triage.

Conclusion: CONCLUSION: In our patient population, there is no statistically significant difference among the three scenarios adopting different hs-cTnI cut-offs in identifying hospitalized patients. There is a statistically significant association observed between the color code given during the triage, the hs-cTnI level and the hospitalization. Therefore, the appropriate use of hs-cTnI assays is the key to the correct diagnosis.
A-091

High-sensitivity cardiac troponin T assay has increased susceptibility to biotin interference

C. Mwangi1, I. Frame2, A. Muthukumar1, 1Clements University Hospital, UT Southwestern Medical Center, Dallas, TX, 2Department of Pathology, UT Southwestern Medical Center, Dallas, TX, 3Department of Pathology and Clements University Hospital, UT Southwestern Medical Center, Dallas, TX

Background: Biotin, vitamin B7, can interfere in assays that have streptavi-din-biotin interaction as a part of their assay reaction. The high-sensitivity cardiac troponin T generation 5 assay (hs-cTnT) now available in the US is one of the assays vulnerable to biotin interference because of its assay design. Given the importance of the hs-cTnT assay in rapidly ruling-in and ruling-out acute myocardial infarction (AMI) in patients presenting with chest pain in the emergency department (ED), we sought to evaluate the extent of biotin interference in the new assay in comparison to the contemporary 4th generation troponin T assay (cTnT). Further we sought to estimate the impact of biotin interference in hs-cTnT in ruling out AMI through simulations based pharmacokinetic studies.

Methods: This was a University hospital, laboratory based study of discarded blood samples received from patients presenting to the ED and referred for troponin measurement. 23 cTnT-positive patient samples were tested by hs-cTnT and cTnT assays after adding known plasma concentrations of biotin achievable from a 5-day course of biotin, 10 mg daily. Maximum plasma biotin concentrations of 140, 100 and 50 ng/ml achievable at 1, 2 and 4 h after the last dose taken on the 5th day were simulated. Next, biotin spiking experiment with a wide range of plasma biotin concentrations (10-2000 ng/ml), as required by the FDA was undertaken in cTnT positive patient samples. In the presence of biotin, false decreases >10% or suppression of cTnT values below the 99th percentile of upper reference limit and/or our institution’s threshold for abnormal (hs-cTnT≥52 ng/L; cTnT≥0.01 ng/ml) were considered significant.

Results: A simulation of daily biotin use in 23 cTnT-positive patient samples resulted in significant interference in hs-cTnT values compared with the cTnT assay. 78% and 33% of hs-cTnT results were falsely decreased below the upper reference level of 19.33% and 5.54% respectively. Among 12 samples that were significantly abnormal (hs-cTnT≥52 ng/L), 83%, 70%, and 29% had values <52 ng/L at 1, 2, and 4 h post-dose biotin simulations, respectively. In contrast, cTnT results remained unaffected at these plasma biotin concentrations. In dose-dependent biotin testing, the hs-cTnT assay was susceptible to biotin interference at plasma biotin >315 ng/ml compared with a threshold >315 ng/ml for the cTnT assay.

Conclusions: Our data suggest a significant risk of false rule-out or delayed rule-in of AMI in the presence of biotin with hs-cTnT, far more than with the prior cTnT assay, at plasma biotin concentrations reflecting those contained in commonly used over-the-counter supplements. We suggest careful history taking for OTC supplements in patients presenting for rule out of AMI using the hs-cTnT assay. We also suggest the manufacturer work to increase the biotin tolerance levels of the assay or convert it to a non-biotinylated assay. Finally, we advise health care systems using this assay to make ordering providers aware of the potential for biotin interference in hs-cTnT levels.

A-092

Performance Evaluation of the VITROS® hs Troponin I Assay® on the VITROS® 5600 Integrated and VITROS® 3600 and ECI/ECQ Immunodiagnostic Systems


Background: The Joint European Society of Cardiology/American College of Cardiology guidelines state that cardiac troponins are the preferred biomarkers for the detection of myocardial injury, for risk stratification in patients diagnosed with acute coronary syndrome, and for the diagnosis of myocardial infarction. Because of the demand for accurate and precise measurement of low troponin levels, there is an increased need for assays with improved analytical performance.

Methods: We are developing a rapid, fully automated high sensitivity assay for the measurement of cardiac Troponin I (cTnI) in human serum and plasma (heparin) for use on the VITROS® Systems. The VITROS® hs Troponin I (hsTnI) assay uses an immunometric technique in which the cTnI present in the sample reacts simultaneously with one streptavidin-conjugated antibody, bound by biotin-BSA on the wells, and a dual antibody-horseradish peroxidase conjugate. The antigen-antibody complex is captured by the antibody coated on the wells. Unbound materials are removed by washing, and the bound HRP conjugate is measured by a lumines-
Cardiac Markers

A-094

Serum Gamma-Glutamyltransferase Levels are Associated with Cardiovascular Risk Factors in China: A Nationwide Population-Based Study

D. Liu, T. Xu, X. Cheng, W. Wu, Y. Ye, X. Guo, Q. Cheng, Q. Liu, L. Liu, G. Zhu, J. Wu, L. Qiu,1 Department of Clinical Laboratory, Peking Union Medical College Hospital, Peking Union Medical College & Chinese Academy of Medical Science, Beijing, China, 2Department of Statistics, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, 3Department of Cardiology, Peking Union Medical College Hospital, Peking Union Medical College & Chinese Academy of Medical Science, Beijing, China, 4Department of Basic Medical Sciences, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

Background: Serum Gamma-Glutamyltransferase (GGT), which is mainly derived from the liver, is a sensitive marker of liver cell damage and oxidative stress. More recently, it has been found that the increased plasma activity of GGT is also associated with cardiovascular disease (CVD). However, data on the relationship between GGT and cardiovascular risk factors (CRFs) are lacking in nationally representative samples of the Chinese population. Here, we aim to investigate both the association between GGT and CRFs and CRFs clustering. Methods: A cross-sectional survey was conducted in a nationally representative sample of 22,827 adults aged 18 years and older from 2009 to 2017, including a plurality of ethnic minorities. Questionnaires and physical examinations were performed, and laboratory measurements were collected. The participants were then divided into quartiles of sex-specific serum GGT. Results: People in Northern and Rural areas tended to have a greater chance of belonging to the upper quartiles of GGT, and for ethnic groups, Mongolians had the highest serum level of GGT. From the low to the high GGT quartile, the incidence of each CRF and clustering risk factors increased after adjusting for uric acid (UA), drinking, ethnicity and all other risk factors. Subjects in the upper stratum (75th percentile) had higher prevalence rates of CRFs than did those in the lower stratum. Furthermore, the individuals with clustering of 1, 2 or ≥3 CRFs were still more likely to belong to the upper GGT quartiles (75th percentiles) than were those without risk factors in both genders. Conclusion: Our data highlight the association between higher serum GGT levels and CRFs in Chinese adults. We found that people with higher serum GGT levels tend to have a greater chance of CRFs and that there was a dose-response association between the number of CRFs and higher serum GGT, especially in men, suggesting that serum GGT may serve as a valuable clinical marker of cardiovascular disease in China. Further studies are needed to elucidate the causality between serum GGT and CRFs and to evaluate the effects of serum GGT lowering therapies on CVD prevention and outcome.

A-095

Sex-specific versus universal clinical decision limits for troponin I and T for the diagnosis of acute myocardial infarction - a systematic review

D. M. Kimeai1, E. B. N. J. Janssen1, K. M. Eggers2, B. Lindahl1, H. M. den Ruiter1, O. Bekers1, Y. Appelman2, J. R. J. Meeuws1, Maarstricht University, Netherlands, Uppsala University, Uppsala, Sweden, 2University Medical Center Utrecht, University of Utrecht, Utrecht, Netherlands, 3VU University Medical Center, Amsterdam, Netherlands

Background: The universal clinical decision limits of high-sensitivity cardiac troponin I (hs-cTnI, 26 ng/L) and T (hs-cTnT, 14 ng/L) may contribute to underdiagnosis of acute myocardial infarction in women. We performed a systematic review to investigate sex-specific and universal 99th percentiles of hs-cTnI and hs-cTnT derived from healthy reference populations. Methods: We searched in PubMed and EMBASE for original studies, and by screening reference lists. Reference populations designed to establish 99th percentiles of hs-cTnI (Abbott) and/or hs-cTnT (Roche), published between January 2009 and October 2017, were included. Sex-specific and universal 99th percentile values of hs-cTnI and hs-cTnT were compared with universal clinical decision ranges (hs-cTnI: 23.3-29.7 ng/L, hs-cTnT: 12.7-24.9 ng/L). Results: A total of 28 studies were included in the systematic review. Of 16 hs-cTnI and 18 hs-cTnT studies, 14 (87.5%) and 11 (61.1%) studies reported lower female-specific hs-cTn cut-offs than universal clinical decision ranges, respectively. Contrary, men-specific thresholds of both hs-cTnI and hs-cTnT were in line with currently used universal thresholds, particularly hs-cTnT (90% concordance). The variation of estimated universal 99th percentiles was much higher for hs-cTnI than hs-cTnT (29.4% versus 80.0% of hs-cTnI and hs-cTnT studies reported values within the current universal clinical decision range, respectively). Conclusion: Our data show substantially lower female-specific upper reference limits of hs-cTnI and hs-cTnT than universal clinical decision limits of 26 ng/L and 14 ng/L, respectively. The statistical approach strongly affects for the hs-cTnT threshold. Downwards adjustment of hs-cTn thresholds in women may be warranted, to reduce underdiagnosis of acute myocardial infarction in women.

A-096

Decision limits, delta troponin or both for the confirmation and exclusion of myocardial infarction using contemporary and high sensitive assays

P. O. Collinson1, D. Gazze2, S. Goodacre3, 1St George's Hospital, London, United Kingdom, 2University of Sheffield, Sheffield, United Kingdom

Objective: To examine the impact of a combination of a delta troponin with different decision limits for the rapid confirmation or exclusion of myocardial infarction (MI). Methods: The study was a sub study of the point of care arm of the RATPAC trial (Randomised Assessment of Treatment using Panel Assay of Cardiac markers), set in the emergency departments of six hospitals. Prospective admissions with chest pain and a non-diagnostic electrocardiogram were randomised to point of care assessment or conventional management. Blood samples were taken on admission and 90 minutes from admission for measurement of a panel of cardiac markers. An additional blood sample was taken at admission and 90 minutes from admission, separated and the serum stored frozen until subsequent analysis. All patients were followed up to 30 days for major adverse cardiac events (MACE). Samples were analysed for cardiac troponin I (cTnI) by the Stratus CS (Siemens Healthcare Diagnostics), range 50-50,000 ng/L; 10% CV 60 ng/L, 99th percentile 70 ng/L; the Beckman AccuTnI enhanced (B) (Access 2, Beckman-Coulter) range 1 - 100,000 ng/L, 10% CV 30 ng/L, 99th percentile 40 ng/L, the Siemens Ultra (S) (ADVIA Centaur, Siemens Healthcare Diagnostics), range 6 - 50,000 ng/L, 10% CV 30 ng/L 99th percentile 50 ng/L, and cardiac troponin T (cTnT) by the Roche high sensitive troponin T (hTnT) (Elecsys 2010, Roche diagnostics), range 3 - 10,000ng/mL, 10% CV 13ng/L, 99th percentile 14 ng/L. The universal definition of myocardial infarction utilising laboratory measurements of cardiac troponin performed at the participating sites together with measurements performed in a core laboratory was used for diagnosis. Myocardial infarction was diagnosed by a value exceeding the 99th percentile and/or the combination of a delta troponin. Myocardial infarction was excluded when either the admission or all values fell below the limit of detection of the assay and there was no delta troponin. All other patients were classed as non-diagnostic. Results: Samples were available from 813 and serial samples in 617/1132 patients enrolled in the study, 60% male, age 23.7-92.8 years median 53.8 years. The admission sample below the limit of detection (LOD) missed 0.6-1.2% of patients. Both samples remaining below the LOD of the assay with no delta change excluded myocardial infarction in 88% of cases and was associated with a MACE rate of 0.2-0.3%, all of which were readmissions with acute coronary syndrome. Use of a delta change did not improve detection of MI but increased the number of false positive diagnoses by 0.1-1.5%. Conclusion: Serial measurements are required for reliable rule out of MI. Troponin below the limit of detection measured with a sensitive or contemporary sensitive assay without a delta change identified a very low risk group who can be considered for immediate further investigation or discharge. The 99th percentile alone on serial sampling was the most effective. Rule in with a delta in addition generated false positive results.

A-097

Study of the association between bone mineral disorders <and> intradialytic hypertension in patients on maintenance hemodialysis

S. S. Naga1, M. N. Mowa2, Y. A. Aamri2, Q. H. Elgaddar1, E. M. Mehan3, M. Magdy1, 1Faculty of Medicine, Alexandria University, Alexandria, Egypt, 2Medical Research Institute, Alexandria University, Alexandria, Egypt

Background: Intradialytic hypertension (ID-HTN) affects up to 15% of hemodialysis (HD) patients and is associated with significant risk of hospitalization and death. Abdominal aortic calcification affects 81% of MHD patients with its severity increases with age, duration of dialysis and history of cardiovascular disease (CVD). Mineral Bone Disease (CKD-MBD) related factors such as serum calcium, phosphorus, and parathyroid hormone are strong-
ly associated with severity of Aortic calcification (AC) in HD patients. GFG-23 level increases progressively in CKD patients, beginning in its early stages achieving the highest values in end-stage renal disease (ESRD) patients, to maintain normal serum phosphate levels. Elevated GFG-23 has been linked with hypertension, left ventricular hypertrophy and increased cardiac mortality in CKD patients, but its role in pathogenesis of ID-HTN via inducing vascular calcification and stiffness remains to be explored.

Methods:
This study included sixty ESRD patients on regular HD for more than 6 months, that were classified into two groups; Group (1): forty five ID-HTN prone HD patients who developed episodes of ID-HTN in more than 2/3 of HD sessions done during last 3 consecutive weeks, and Group (2): fifteen hemodynamically stable (S) HD patients, without history of ID-HTN as a control group. To all subjects, laboratory investigations were performed including pre- dialysis serum urea, creatinine, electrolytes, minerals, iPTH and FG23. Abdominal aortic calcification score (AACS) was assessed in lateral abdominal radiographs by Kauppi method. Atherosclerosis score (AS) was calculated based on measurement of carotid intima media thickness (CIMT), detection of carotid plaques with or without significant stenosis and measurement of ankle brachial BP index.

Results:
Hypertension prone (HP) patients had significantly longer duration of dialysis and higher AACS compared with hemodynamically stable (S) patients. Serum phosphorus, calcium phosphorus product (CaPhP), iPTH and FG23 were higher in HP than S patients, but the difference was not statistically significant. There was a statistically significant positive correlation between FG23 and each of duration of dialysis (P = 0.003) and CIMT (P = 0.043). Moreover, AS had a statistically significant positive correlation with serum calcium (P = 0.009).

Conclusion:
The occurrence of ID-HTN is associated with significantly more advanced vascular calcification and fairly increased levels of humoral MBD mediators involved in this process like FG23, iPTH and CaPhP. FG23 significantly correlates with CIMT, possibly indicating its involvement in the atherosclerotic process from the early beginning. It remains to be elucidated whether interventions to control FG23 rise and other MBD parameters would reduce ID-HTN episodes.

A-099

Analytical Evaluation of a New Ultra-Sensitivity Troponin I Assay using Human Serum
T. G. Morris, D. C. Gaze, P. O. Collinson, St George's University Hospitals NHS Foundation Trust, London, United Kingdom

Background: The universal definition of acute myocardial infarction (AMI) puts cardiac troponin at the forefront of diagnosis. With the advent of high-sensitivity assays for cardiac troponins the diagnosis of AMI can be made sooner with a higher degree of confidence. The objective of this study was to provide an analytical evaluation of a newly developed ultra-sensitivity cardiac troponin I assay (us-cTnI), using serum samples.

Methods: Us-cTnI was measured using the Sgx Clarity™ cTnl Assay (us-TnIavian) via the Singulex Clarity System, with a reported limit of detection (LoD) of 0.08 ng/L and a 99th percentile upper reference limit (URL) of 8.67 ng/L in EDTA plasma. The us-TnIavian limit of blank (LoB) and LoD were calculated in this study after measuring the zero calibrator 22 times. Imprecision profile, linearity and sample stability were determined using pooled human serum samples. A sample type comparison was performed with paired serum and EDTA plasma. The 99th percentile URL was calculated with serum from 638 apparently healthy individuals (318 females and 320 males) using the Harrell-Davis quantile bootstrap statistical method. Receiver operating characteristic (ROC) curves were used to compare the clinical performance of the us-TnIavian with the hs-cTnT (Abbot), and hs-cTnT (Abbot) assays in a limited study using serum; the hs-cTnT (Abbot) and hs-cTnT (Abbot) were measured by using serum samples.

Results: The hs-cTnT (Abbot) assay had LoD of 11.9-1.9 ng/L and a 10% CV of 4.7 ng/L; the hs-cTnT (Abbot) assay had a LoD of 5 ng/L and a 10% CV of 13 ng/L.

Conclusion: The us-Tnlavian assay had a LoB, LoD and 10% CV lower than any other assay currently on the market, making it the most sensitive cardiac troponin assay available. Sample stability was acceptable enough to allow both clinical and research applications. There was a matrix effect in serum when compared to EDTA plasma. The 99th percentile URL in serum was lower than that reported in EDTA plasma, which likely reflects differences in the underlying reference populations. There was an expected male/female difference in serum 99th percentile URL. Clinical diagnostic performance of the us-Tnlavian assay appeared better than the predicate assays tested.

A-098

Simultaneous Assessment of N-terminal pro-B-type Natriuretic Peptide and Prespisin Improves Risk Prediction of Acute Kidney Injury and Mortality after Cardiac Surgery
E. Spanuh1, H. Bomberg2, M. Klingele1, R. Thoma2, H. Groesdonk2, D. Di-Anering GmbH, Heidelberg, Germany, 1Department of Anaesthesiology, Intensive Care Medicine and Pain Medicine, Saarland University, University Medical Centre, Homburg/Saar, Germany, 2Department of Medicine, Division of Nephrology and Hypertension, Saarland University, University Medical Centre, Homburg/Saar, Germany, 3Mitsubishi Chemical GmbH, Düsseldorf, Germany

Background
Acute kidney injury (AKI) is common after cardiac surgery. Also sepsis has shown to contribute to the development of AKI in intensive care patients. Prespisin (PSEP) has proven as a marker with high diagnostic and prognostic validity in assessment of disease severity and association to kidney function in septic patients. N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels reflect cardiac filling pressures. Therefore NT-proBNP is a surrogate marker for hemodynamic status. It has been shown association of NT-proBNP with AKI and cardiac events after cardiac surgery.

Objective
The aim of the present study was to evaluate the diagnostic validity of NT-proBNP and PSEP to predict the risk of cardiac surgery-associated AKI (CSA-AKI) and postoperative mortality in comparison with the inflammatory markers C-reactive Protein (CRP) and procalcitonin (PCT) and creatinine.

Methods
The marker concentrations were measured in plasma samples which were drawn in the early morning after surgery from 856 patients undergoing elective cardiac surgery. Outcome measures were postsurgical AKI during hospitalisation and mortality. PSEP and NT-proBNP were determined by using PATHFAST Prespisin (LSI Medience corporation, Tokyo) and Eleeys NT-proBNP (Roche Diagnostics). CRP, PCT and creatinine were measured using routine clinical chemistry methods in the central laboratory.

Results
Patients who developed AKI (n=221, 25.8%) had higher PSEP and NT-proBNP levels than patients without AKI (PSEP: 632 ng/L [IQR 378-1069] versus 304 ng/L [228-519]; P<0.001; NT-proBNP: 1594 ng/L [IQR 667-3838] versus 352 ng/L [IQR 122-1084]; P<0.001. The results for 6-month death (n=49, 5.8%) were: PSEP: 337 ng/L [IQR 246-512] versus 1081 (511-1962), Difference 744 ng/L; P<0.001 and NT-proBNP: 499 ng/L [IQR 161-1475] versus 2632 ng/L [IQR 1308-3874], Difference 2133 ng/L; P<0.001 for survivors versus non-survivors, respectively. AKI has been assessed according to AKIN classification: stages 1 (n=122), 2 (n=54), 3 (n=45). The marker concentrations increased significantly from AKIN 1 to 3. Receiver operator curve (ROC) analysis for prediction of 6-month death revealed AUC values of 0.792 and 0.847 for NT-proBNP and PSEP compared to AUC values of 0.670, 0.778 and 0.639 for creatinine, PCT and CRP, respectively. Similar results were obtained for prediction of postsurgical AKI by ROC analysis. AUC values were 0.758 and 0.783 for NT-proBNP and PSEP, compared to AUC values of 0.671, 0.671 and 0.512 for creatinine, PCT and CRP, respectively. Examination of the predictive value of marker combinations by logistic regression revealed an AUC value of 0.796 for the combination PSEP and NT-proBNP versus 0.671, 0.671 and 0.512 for creatinine, PCT and CRP, respectively. A similar finding was obtained for the prediction of postsurgical AKI compared to all other possible marker combinations.

Conclusion
NT-proBNP and PSEP demonstrated comparable predictive power for risk of 6-month mortality after cardiac surgery and to identify patients who were at risk of developing CSA-AKI. Moreover, the combination of both markers was found to improve the prognostic performance. The simultaneous assessment of NT-proBNP and PSEP allows early risk prediction of AKI already at the first day after surgery and may enable individual risk stratification with appropriate individualized patient care.
The implementation of the high sensitivity Troponin T (hs-TnT) generation five assay at a large teaching county hospital. A multi-specialty effort

L.A. Hashmi1, F. Fernandez2, A. Yel3, B. Bertulfo4, S. Das1, D. Dierckx1, J. DeLemos1, P. Kutcher2. 1University of Texas Southwestern Medical Center, Dallas, TX, 2Parkland Health & Hospital System, Dallas, TX

Background

A highly sensitive Troponin T assay (hs-TnT) was recently approved by the FDA for clinical use. In addition to the assay’s much improved sensitivity, the reporting units, reference intervals and critical limits for notification are markedly different. Furthermore, current acute myocardial infarction (AMI) rule out protocol requires serial samples and monitoring for up to 6 hours and it is not known if adopting hs-TnT will impact the protocol. This report describes the implementation of the hs-TnT assay at a large teaching county hospital.

Methods

A multi-specialty team from Clinical Chemistry, Laboratory Administration and Information Technology support services, Nursing, Cardiology, Hospitalists, Performance Improvement and Emergency departments was set up. The hs-TnT assay was validated per protocol on the Cobas® 6000 system, e601 immunoanalyzer (Roche Diagnostics) for analytical performance. Samples received into the laboratory from patients being investigated for acute coronary syndrome were analysed using the conventional 4th generation TnT assay and results reported in the usual manner. The Fifth generation hs-TnT was also measured but results not reported to the electronic medical record. The imprecision of the assay was assessed at recommended decision levels. A new test code was set up in the Laboratory Information System, for the hs-TnT with test specific parameters for measurements limits and critical value. At three months of data and clinical correlation, educational materials were prepared and training sessions conducted for pathology residents and staff, nursing staff, and medical staff, by the clinical chemist, nursing education, and cardiologists respectively.

Results:

969 samples from 541 patients (56% men, 44% women) being investigated for acute coronary syndrome were analysed for both conventional and fifth generation hs-TnT. There was no numerical correlation between the two assays on admission (P=0.39). Laboratory results of both assays correlated well when using clinical assessment of patients. A two step one hour and 3 hours rule-out protocol was developed. The imprecision of the hs-TnT assay ranged from 0% at 12.0 ng/L, 3.3% at 16.4 ng/L, 2.2% at 24.4, 2.1% at 42.6 ng/L, and 0.9% at 60 ng/L. Training sessions were completed on time and educational material circulated through the hospital units and made available through the electronic laboratory handbook. The implementation was done in 2 steps: first phase targeted the Rapid Response Lab performing over 5,000 Troponin tests a month serving the critical care areas. A second phase, 6 weeks later, added the Core Lab supporting the inpatient non-critical units and the outpatient clinic.

Conclusion:

Manufacturer’s claim for assay performance was successfully verified. The imprecision of the assay was acceptable at the established decision limits rule out (<6 ng/L) and a delta of 3 ng/L on serial samples. A real-world pre-implementation scenario was conducted where samples were assayed for both conventional and 5th generation hs-TnT to assess potential impact on patients, and on current and new protocols. This provided the basis for educational material needed to support the implementation.

LC-MS quantification of BNP in plasma without immuno-enrichment

M. S. Lowenthal, K. W. Phinney. NIST, Gaithersburg, MD

Background:

B-type natriuretic peptide (BNP) is a cardiac hormone routinely measured in clinical laboratories to rule-out acute heart failure, and for screening or prognosis of heart failure. However, interpretation of BNP levels is not useful as a “rule-in” marker due to poor positive predictive value. The primary analytical technique used for BNP quantification in the clinic is the immunoassay, which is reported to show significant discrepancies among platforms due to several factors, including non-specificity of antibodies, heterogeneity of patient proteomes, and patient phenotype. As yet, no attempts have been made to harmonize or standardize these clinical immunoassays through use of reference standards and the development of higher order approaches such as isotope dilution mass spectrometry (ID MS). BNP is found at exceedingly low serum concentrations, justifying an immuno-enrichment step prior to detection. One recent report detailing an antibody-free approach to quantifying plasma-spiked synthetic BNP allows for the possibility of achieving absolute quantification of BNP from patient matrix. In addition to abundance, stability is also a major concern for BNP quantification as the active form BNPa is known to metabolize through numerous biochemical and enzymatic routes. At least 15 metabolites of BNPa are known in blood of various chain lengths. This heterogeneity constitutes a major contribution of immunoassay variability. Here, isotope-labeled standards and LC-MS techniques have been used to measure BNPa and its metabolites and estimate their stabilities in plasma. Further efforts have been made detect pre-spiked BNP at clinically-defined “healthy” levels using mass spectrometry in both intact and in vitro digested BNP, as well as native BNPa in “diseased” patient samples.

Methods:

Isotopically-labeled and non-labeled synthetic, intact BNP standards were used for relative quantification of BNP metabolites using a targeted LC-MS/MS (MRM) approach. Isotopically-labeled and non-labeled synthetic tryptic peptides of BNP, were used for estimating “total” BNP through a bottom-up technique, also based on LC-MRM-MS. An organic extraction pre-enrichment method and cleanup was optimized to measure BNPa in clinically-obtained patient sera. This antibody-free approach permits use of an appropriate calibration system for the higher-order quantification of BNP.

Results:

An LC-MS/MS MRM method was optimized for quantification of BNPa and 14 metabolites. BNPa was shown to degrade rapidly in plasma (< 1% remaining after 2 hours). Other metabolites exhibited interesting kinetics, growing-in and degrading at various rates. Interestingly, “shared” tryptic peptides summed from all BNP metabolites were demonstrated to decrease slowly in abundance over time, suggesting possible unknown routes of BNP degradation. Synthetic BNP pre-spiked and extracted from plasma was detected down to <100 attomoles by LC-MS techniques, adequate for quantification at clinical levels. Native BNP
from patient sera was subsequently tested using the optimized LC-MS approach.

**Conclusion:**
Extending an antibody-free ID MS approach to the quantification of native BNP in plasma is necessary for development of the appropriate calibration system and measurement standards required to harmonize clinical immunoassays.

**A-103**

**Susceptibility of High Sensitivity Cardiac Troponin I and Gen 5 cTnT Assays to Biotin Interference**

I. L. Gunsolus\(^1\), A. Muthukumar\(^2\), J. Nicholson\(^1\), C. Mills\(^1\), R. Ler\(^1\), K. Schulz\(^2\), A. Sexter\(^1\), I. Frame\(^1\), F. S. Apple\(^1\), \(^1\)Hennepin County Medical Center, Minneapolis, MN, \(^2\)UT Southwestern Medical Center, Dallas, TX

**Background:** The FDA has alerted clinicians, laboratory personnel, and manufacturers of immunoassays that patient ingestion of high levels of biotin in dietary supplements can cause clinically significant incorrect lab test results. Depending on a test assay’s configuration, increased biotin in patient samples can cause falsely high or low results. Our objective was to examine the susceptibility of two cardiac high-sensitivity troponin (hs-cTn) assays used globally in clinical practice to biotin supplementation.

**Methods:** Four experiments were performed using excess, discarded lithium heparin plasma from patients with a positive cTnT (Roche 4th Gen) concentration. Overall, 133 specimens were analyzed by both the Abbott (investigational in US) hs-cTnT, Architect i2000, and Roche Gen 5 cTnT (cobas e601; FDA version of hs-cTnT used globally) assays. First, positive cTnT specimens (n=16) were titrated against a range of biotin levels (0-140 ng/mL) by simulating 1, 2, and 4-hour post-dose plasma biotin levels achievable for daily dose of 10 mg taken for 5 days. Second, the effect of mega doses of biotin (500 and 1000 ng/mL) was tested (n=10). Third, biotin levels were titrated against a range of biotin levels between 0 and 2000 ng/mL (n=12). Fourth, the effectiveness of streptavidin beads in blocking biotin that had been spiked into patient samples (n=3) was tested. Spiked samples with known levels of biotin (100 and 500 ng/mL) followed by blocking with 50 µL of streptavidin beads. The samples were then incubated at room temperature for 1 hour with intermitting shaking, centrifuged, and the supernatant was taken for cTnT testing. False decreases at >10% or suppression of values below the 99th percentile URL (Gen 5 cTnT 16 ng/L, hs-cTnT 18 ng/L) in the presence of biotin were considered significant.

**Results:** hs-cTnT concentration suppression crossed the 10% threshold at a 35 ng/mL biotin level. hs-cTnT concentrations were suppressed 24%, 50%, 78% and >90% at 50, 100, 140 and 500 ng/mL biotin levels, while hs-cTnI concentrations were <8% suppressed at all levels. 4%, 25%, 43% and 62% of hs-cTnT levels, respectively, were suppressed from increased to below the 99th percentile URL. Blocking with streptavidin beads eliminated hs-cTnT concentration suppression from 59% at 100 ng/L biotin and 95% at 500 ng/mL biotin levels to <7%. Conclusions: The Gen 5 cTnT assay that uses a sandwich immunoassay with biotinylated antibodies experienced significant negative interference with biotin concentrations at >35 ng/mL, that could result in false negative concentrations. The hs-cTnI assay was free from biotin interference at all concentrations tested.

**A-104**

**Highly Sensitive Cardiac Troponin Assay: Experience at a US Academic Medical Center**

J. A. Hubbard\(^1\), L. B. Daniels\(^2\), V. Tolia\(^2\), R. L. Fitzgerald\(^2\), \(^1\)University of California, San Diego, San Diego, CA, \(^2\)UC San Diego Health, San Diego, CA

**Background:** About 6 million patients present to the Emergency Department (ED) each year with complaints of chest pain. Of those, about 1.5 million rule in as having an acute myocardial infarction (MI). A key component of diagnosis is the rise and fall (>20%) of cardiac troponin (cTn), a highly sensitive and specific biomarker. A highly sensitive generation 5 (gen5) cTn assay has been in use in Europe and parts of Asia for over 10 years, but this was not clinically available in the United States. Recently, the FDA approved the gen5 assay for use within the U.S. In this study, the performance of a generation 4 (gen4) cardiac troponin (cTnT) assay was compared to the highly sensitive gen5 cTnT assay for the first time within a US healthcare system.

**Methods:** Over a two-month period, all patients within University of California, San Diego (UCSD) Health in whom cTnT was ordered had both gen4 and gen5 measured. A total of 4,809 troponin orders from 2,516 patients (1,185 female and 1,211 male) were analyzed, giving an average of 1.9 troponin orders per patient.

**Results:** The correlation between gen4 and gen5 (R\(^2\)) was 0.99 and 0.98 for male and female patients, respectively. The gen4-cTnT assay detected cTnT levels down to 0.01 ng/mL whereas the highly sensitive gen5 assay detected levels down to 0.006 ng/mL. (6 ng/L). This increased sensitivity allowed for the detection of cTnT in 81% of samples (3879/4809) analyzed by the gen5 assay, whereas gen4 only detected cTnT in 33% of samples (1572/4809). Any detectable level of cTnT (>0.01 ng/mL) using the gen4 assay was considered elevated. When using the gen5 sex-specific 99th percentile cutoffs of 14 ng/L for females and 22 ng/L for males, a total of 871 samples from 565 patients were positive by the gen5 assay but had undetectable levels by gen4. Many of these patients (302) had only a single troponin order, while 167 had at least a second cTnT ordered within 8 hours of the initial measurement. Of these 167 patients, 119 exhibited a stable elevation of cTnT by gen5 and 35 were detected by both gen4 and gen5 in the serial measurement. A total of 13 patients, however, exhibited >20% change in gen5 while remaining undetectable in gen4. Of these cases, 3 patients were diagnosed with a non-ST-elevation MI (NSTEMI) and 2 with an ST-segment elevation MI. Two of the NSTEMI patients demonstrated a >20% elevation in cTnT using the gen5 assay before it was detected by gen4.

**Conclusion:** The initial experience at UCSD Health was that gen5 cTnT detected elevations of cTnT in significantly more patients than the gen4 assay. The majority of these patients had stable elevations of cTnT. During this two month evaluation, gen5 cTnT detected a >20% changes in cTnT prior to detection by gen4 in several patients. These results confirm the importance of monitoring serial changes in time when implementing highly sensitive troponin assays and suggest that gen5 cTnT will allow for a faster rule-out protocol.

**A-105**

**Quantifying the prevalence of elevated biotin in a cohort with suspected acute coronary syndrome**

B. Mumma\(^1\), D. Diercks\(^2\), A. Ziegler\(^3\), C. Dinkel-Keuthage\(^4\), N. Tran\(^1\), \(^1\)UC Davis Medical Center, Sacramento, CA, \(^2\)UT Southwestern Medical Center, Dallas, TX, \(^3\)Roche Diagnostics International Ltd, Rotkreuz, Switzerland, \(^4\)Roche Diagnostics GmbH, Penzberg, Germany

**Background:** Biotin can reduce recovery of the Elecsys® Troponin T Gen 5 (TnT Gen 5) assay at concentrations >20ng/mL (99% recovery), potentially leading to false-negative prediction of acute myocardial infarction (AMI). We aimed to determine the prevalence of biotin concentrations >20ng/mL and the 99th percentile biotin concentration in the intended use population.

**Methods:** Biotin was quantified using an in-house assay (lower limit of detection: 0.1ng/mL) in residual 0-hour and 3-hour blood samples from 850 patients presenting to 15 US emergency departments with suspected AMI from July 2014 to October 2015. Potential impact of biotin on the negative predictive value (NPV) of the TnT Gen 5 assay and likelihood of false-negative AMI prediction was estimated at biotin concentrations 3 times the highest observed concentration (per Clinical and Laboratory Standards Institute [CLSI] EP07).

**Results:** The 99th percentile biotin concentration for 0-hour samples was 2.62ng/mL and for 3-hour samples was 2.38ng/mL. These values are >7 times lower than the TnT Gen 5 assay interference threshold (conforming with CLSI EP07 criteria). Biotin was >20ng/mL in 1/797 (0.13% 95% confidence interval [CI] 0-0.70%) 0-hour and 1/646 (0.15%; 95% CI 0-0.86%) 3-hour samples (30.23ng/mL and 24.48ng/mL, respectively); both samples were from the same patient. Based on extreme biotin assumptions derived from the study population (0.7% prevalence of 0-hour biotin up to 100ng/mL; maximal reduction in troponin recovery of 42% at 100ng/mL; 15% prevalence of AMI), 0-hour TnT Gen 5 results between 1ng/L and 45.24ng/L could potentially lead to false-negative AMI prediction. As 25% of patients with AMI had 0-hour results within this range, the likelihood of false-negative results due to biotin interference was estimated as 0.026% (Figure).

**Conclusion:** Our results suggest biotin interference has a minimal effect on the NPV of the TnT Gen 5 assay and should not change current clinical practice.
Baseline High-Sensitivity Cardiac Troponin I Aids in Risk Assessment in Patients with Diabetes, Hypertension, and Dyslipidemia without Myocardial Infarction

L. L. Gunsolus1, Y. Sandoval1, S. W. Smith1, A. Sexter2, K. Schulz1, S. F. Apple3,1, Department of Laboratory Medicine and Pathology, Hennepin County Medical Center, Minneapolis, MN, 1Department of Cardiology, Mayo Clinic, Rochester, MN, 2Department of Emergency Medicine, Hennepin County Medical Center, Minneapolis, MN, 3Chronic Disease Research Group of Minneapolis Medical Research Foundation, Minneapolis, MN, 4Minneapolis Medical Research Foundation, Minneapolis, MN, 5Department of Laboratory Medicine and Pathology, Hennepin County Medical Center, University of Minnesota, Minneapolis, MN

Background: Cardiac troponin has been shown to be a powerful prognostic biomarker for patients both with and without acute coronary syndromes. The objective of our study was to determine use of baseline high-sensitivity cardiac troponin I (hs-cTnI) concentrations for the risk stratification of patients with diabetes, hypertension, and dyslipidemia among emergency department patients without acute myocardial infarction.

Methods: Prospective, observational cohort study (UTROPIA) including patients presenting to a United States emergency department in whom high sensitivity hs-cTnI concentrations were measured on clinical indication using an investigational assay (Abbott, 99th percentile URLs: males 34 ng/L and females 16 ng/L). Patients with myocardial infarction (n=168) were excluded. We assessed the impact of comorbidities across the entire cohort for each hs-cTnI tertile. Outcomes examined were 180-day mortality and major adverse cardiac events (MACE).

Results: Among 1,463 patients, 436 (30%) had diabetes, 947 (65%) had hypertension, and 707 (48%) had dyslipidemia. Tertiles showed a higher risk for 180-day mortality and MACE, with increasing tertile mortality and MACE in the entire cohort (mortality: no comorbidities: 3.7%, T2: 8.9%, T3: 23.5%). Cumulative comorbidities increased the risk for 180-day mortality and MACE rates were 0.5% when no comorbidities were present compared to 1.6% and 3.2%, respectively, when at least one comorbidity was present. Conclusions: Baseline hs-cTnI concentrations aid in the risk assessment of patients with diabetes, hypertension, and dyslipidemia, even without myocardial infarction; patients with higher hs-cTnI concentrations are at higher risk than those with lower concentrations. The cumulative presence of comorbidities increased the risk of adverse events and the presence of ≥2 comorbidity increased the risk for adverse events even in those with very low hs-cTnI concentrations.
with an eGFR < 60 ml/min had significantly lower concordance (70%, kappa 0.636) than those with eGFR > 60 ml/min (77%, kappa 0.731). Moreover, the mean ratio of NT-proBNP to BNP was significantly higher in patients with CKD (10.7:1) than in non-CKD patients (5.7:1). Consequently, there was significantly greater correlation between NT-proBNP and BNP concentrations in patients with eGFR > 60 (r² = .717) than patients with eGFR < 60 (r² = .581) in the acute setting. Finally, for patients with multiple measurements of natriuretic peptides, there was variability between changes in BNP relative to changes in NT-proBNP concentrations over time. Overall, 20% of paired temporal measurements had an inverse relationship (increase in one peptide and a decrease in the other). Together these data showed surprising differences in diagnostic concordance and monitoring values between BNP and NT-proBNP, particularly among patients with CKD. We conclude that using the current cutoffs for heart failure, concentrations of NT-proBNP and BNP have surprisingly poor diagnostic concordance. Further studies are required to examine the diagnostic concentrations of natriuretic peptides, modes of clearance, and assay specificity for the multiple circulating forms of natriuretic peptides.

A-109

Analytical Comparison of High Sensitivity Cardiac Troponin I and T Assays in Patients Presenting to the Emergency Department - the CONTRAST Study

F. S. Apple1, Y. Sandoval1, S. Smith1, A. Jaffé1, N. Mills1, S. Love1, A. Saenger1, A. Sexter1, J. Nicholson1, K. Schulz1, Hennepin County Medical Center, Minneapolis, MN, 2Mayo Clinic, Rochester, MN, 3The University of Edinburgh, Edinburgh, United Kingdom, 4University of Minnesota, Minneapolis, MN

Background: This study compared the frequency of increases in high-sensitivity cardiac troponin (hs-cTnI) I, hs-cTnT, and contemporary cTn assay performances in patients being evaluated in a US emergency department undergoing cTn measurements on clinical indication. Objectives were to determine the concordance of positive and negative results based on sex-specific 99th percentile upper reference limits (URLs) and correlations between hs-cTn assays and a contemporary assay. Methods: This analytical sub-study examined plasma (EDTA) specimens (n=1,000) randomly selected from >9,000 specimens from patients enrolled in the 'Comparison of High Sensitivity Cardiac TropoIn 1 and T Assays' (CONTRAST) study (clinicaltrials.gov NCT03214029). Patient clinical information was not included nor was available to determine whether single or multiple serial specimens from the same patient were included. Fresh specimens were measured by the hs-cTn Abbott Architect assay and the Gen5 cTnRoche cobas e601 assay after completion of clinical testing with the contemporary cTn (Abbott). Two sex-specific 99th percentiles were used to evaluate each hs-assay: manufacturer’s package inserts (PI) and 99th percentile URLs derived from the AACC’s Universal Sample Bank (USB), were: Abbott, PI - M 34 ng/L, W 16 ng/L; USB - M 19 ng/L, W 10 ng/L; Roche PI - M 22 ng/L, W 14 ng/L; USB M 16 ng/L, W 10 ng/L. The 99th percentile URL of the contemporary assay was 0.03 μg/L. The values of all assays were plotted and described using Pearson’s correlation coefficients (r value) with Fisher’s 95% confidence intervals (CI). Proportions of increased results were cross-tabulated to determine agreement with the Kappa statistic. Results: Using PI URLs, the percentage of specimens above the 99th percentile was 30% for hs-cTnI and 47.4% for Gen 5 cTnT. For comparison, using the lower USB URLs increased the percentage of increased results to 40.6% for hs-cTnI and 55.5% for Gen 5 cTnT. Using the PI URLs, 94.3% of Gen 5 cTnT results were greater than the 99th percentile in specimens with increased hs-cTnI results. In comparison, only 59.5% of hs-cTnT results were increased in specimens that had increased Gen 5 cTnI results; kappa of 0.575 (95%CI, 0.507, 0.623). A similar difference in cross-assay increased rate was also observed using the USB URLs. Compared to a rate of increased contemporary cTnT results of 31.1%, using the PI hs-assays URLs, there was a 3.6% decrease in hs-cTnI increases compared to a 52.4% increase in Gen 5 cTnT increases. The Pearson correlation coefficient between the hs-cTnI and hs-cTnT assays was 0.298 (CI 0.241,0.354). Conclusions: Our findings demonstrate substantial differences between the hs-cTnI and Gen 5 cTnT assays in the proportion of values above the sex-specific 99th percentiles, regardless of the URL used. There were greater numbers of increased values for both assays using the lower USB 99th percentile URLs, and for Gen 5 cTnT for both URLs compared to the hs-cTnI assay. Furthermore, there was a substantial increase in the proportion of increased values found between the contemporary cTn assay and the Gen 5 cTnT assay; with a small decrease found for the hs-cTnI assay.

A-110

Race- and Sex- Dependent Association of BNP and Galectin-3 Levels with 6-Month All-Cause Mortality in Patients with Elevated BNP

Y. Wang1, Y. Zhu1, G. Singh1, Inform Diagnostics, Phoenix, AZ, 2Penn State University Hershey Medical Center, Hershey, PA, 3Department of Pathology, Medical College of Georgia at Augusta University, Augusta, GA

Background: B-type natriuretic peptide (BNP) and galectin-3 (Gal-3) are recognized as outcome-predicting factors for heart failure patients, with increased risks of death in the presence of low hemoglobin (Hb) or high creatinine. This study aims to evaluate the association of serum BNP and Gal-3 levels with 6-month prognosis of patients with elevated BNP. Methods: A total of 710 patients (ages 18 or older) from two medical centers with BNP>100 ng/mL at admission were enrolled in this study. A reflex testing of Gal-3 was then performed via the Abbott Architect immunoassay, Hb and serum creatinine concentrations at admission, the occurrences of re-admissions and death within 6 months from the first discharge were retrieved via patient chart review. The biomarker levels, all-cause death rates, days to re-admissions, and re-admission frequencies were compared among different races (white/black), sexes (male/female), and quartiles groups based on BNP and/or Gal-3 levels. The relationship between biomarkers and mortality was assessed via correlation and multivariate regression analysis (MRV). Results: Black patients had significantly higher levels of Gal-3, creatinine, and Hb than white patients. Male patients had greater levels of Gal-3 and Hb than female patients. However, similar BNP levels, death rates, days to re-admissions, and re-admission frequencies were observed in patients with different races or sexes. When patients were divided into 4 subgroups according to the quartiles of their BNP levels, significantly higher death rates (2-5 times) were only observed in white or male patients in the highest BNP quartile (Q4: 4936.6-21375.1 ng/mL vs. Q1: 101.2-196.4 ng/mL). Additionally, the 30-day and 6-month re-admission frequencies were 2 times higher in BNP Q4 than Q1 in white and black patients, respectively. On the contrary, death rates of patients in higher Gal-3 quartiles (Q3: > 26.0-38.3 ng/mL and Q4: >38.3-180.1 ng/mL) were 2-10 times greater than those in Q1 (8.4-19.0 ng/mL) irrespective of race and sex. Patients with higher Gal-3 (Q3 or Q4 vs. Q1) also had a higher 30-day readmission frequency, with no difference between different races or sexes. No additional increase in mortality or re-admission rates was observed when BNP and Gal-3 quartiles were combined. Correlation analysis revealed positive association between death and creatinine in white females (R = 0.254), but negative correlation with Hb in black males (R = -0.264). Moreover, Gal-3 showed strong positive correlation with creatinine (R = 0.571), weak positive association with BNP (R = 0.275), but negative association with Hb (R = -0.302) in all patients. MRV analysis showed that Gal-3 was the only significant variable in the all-cause mortality of all patients, which together with creatinine and Hb formulate a linear regression to predict the death in black male patients (Mortality = 0.005XGal-3 - 0.023XHB - 0.033XCreatinine, p<0.05). In contrast, BNP was only associated with the mortality in white patients (p = 0.018). Conclusion: Our data suggest the race- and sex-dependent association between BNP and Gal-3 6-month all-cause mortality in patients with elevated BNP. In addition to BNP, Hb and creatinine, Gal-3 measurement may provide extra value for predicting all-cause mortality, especially in black male patients.

A-111

A Single High Sensitivity Cardiac Troponin I Measurement From Siemens Healthineers Can Be Used to Rule Out Acute Myocardial Infarction at Low Risk in Patients Presenting to the Emergency Department

F. S. Apple1, R. Christenson2, C. DeFilipp1, J. McCord3, A. Sexter4, R. Nowak5, Hennepin County Medical Center, Minneapolis, MN, 2Department of Pathology, University of Maryland School of Medicine, Baltimore, MD, 3Hennepin Heart and Vascular Institute, Evens Church, VA, 4Henry Ford Heart and Vascular Institute, Henry Ford Health System, Detroit, MI, 5Henry Ford Hospital, Detroit, MI

Background: High sensitivity cardiac troponin (hs-cTn) assays are able to quantify low concentrations of cTn and provide an opportunity to rule out acute myocardial infarction (MI) at an early stage following a patient’s presentation to an emergency department. The objectives of the current study were to examine the performance of single hs-cTn measurement strategy to rule out acute MI and predict 30-day safety outcomes at presentation in these patients. Methods: This was a prospective, observational study of patients (n = 2333). Patient clinical information was not included nor was recognized as outcome-predicting factors for heart failure patients, with increased risks of death in the presence of low hemoglobin (Hb) or high creatinine.
were obtained using the investigational ADVIA Centaur XPT TNH (hs-cTnI) Assay (Siemens Healthcare Diagnostics Inc.). Clinical data and hs-cTnI results were analyzed to determine: 1) clinical sensitivity and negative predictive value (NPV) for ruling out acute MI and 2) safety outcomes of acute MI and death at 30 days, using the hs-cTnI limit of detection (LoD) 1.6 ng/L concentration. Results: In patients with a hs-cTnI <LoD (n=376, 16.1%), the clinical sensitivity and negative predictive value (NPV) for acute MI were 100% (95% CI 98.8,100) and 100% (CI 99.0,100), respectively. Further, the sensitivity and NPV for the safety outcome of acute MI or death within 30 days for hs-cTnI <LoD were 99.7% (CI 99.1,100) and 99.7% (CI 99.2,100), respectively. One patient out of 376 (0.26%) had an event within 30 days. Conclusion: A strategy of using a single hs-cTnI <LoD at presentation allowed the immediate identification of 16.1% of patients highly unlikely to have acute MI and who were at very low risk for events at 30 days. Additional study to understand the clinical utility and cost-savings of this strategy is needed.

A-112

Red Cell Distribution Width and Cardiovascular Risk: four-year follow up of Longitudinal Study of Adult Health (ELSA-Brasil)

N. M. Carvalho, C. B. Maluf, D. R. M. Azevedo, S. M. Barreto, P. G. Vidi, N. M. Carvalho, C. B. Maluf, D. R. M. Azevedo, S. M. Barreto, P. G. Vidi, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Background: Red Cell Distribution Width (RDW) is a quantitative laboratory test that measure the variability in the size of circulating erythrocytes. RDW is easily obtained with automated hematology analyzers, as part of complete blood count (CBC), and is generally used as an indicator of the differential diagnosis of microcytic anemia. Recent studies have shown that RDW is a predictive, diagnostic, and prognostic marker of mortality and cardiovascular events in general population as well as in patients with cardiovascular diseases (CVD). Although pathophysiological mechanisms are still unclear, the evidence obtained so far encourages further research on the RDW in different populations and clinical settings. The aim of this study was to investigate the relationship of the RDW at the baseline of the study with the risk of CVD risk at four years of follow-up in participants of the Longitudinal Study of Adult Health (ELSA-Brasil).

Methods: We used baseline (2008-2010) and second visit (2012- 2014) data of 4471 civil servants enrolled in the ELSA-Brasil cohort. Mixed linear regression model for longitudinal data was used to determine association between RDW and increased cardiovascular risk based on Framingham Risk Score (FRS). RDW were quantified by coefficient of variation of red blood cells volume (RDW-CV%) using XE 2100 D hematologic analyzers (Sysmex, Kobe, Japan), that use impedance technology to estimate particle count and volume. The distribution was distributed according to their exposure to different risk factors, and stratified for cardiovascular risk, based on FRS. Results: RDW (adjusted r²=0.921; p<0.001) was independently associated with the FRS after adjustment for education, skin color, body mass index, abdominal waist circumference, bariatric surgery, hemoglobin concentration, mean corpuscular volume, platelets, C-reactive protein, alcohol consumption. It was observed that a one-unit increase in RDW increases the FRS by 14%, in average. Conclusion: In this large cohort of free living Brazilians, ours results showed that RDW is independently associated with increased CVD risk based on the FRS at four-year follow up. The RDW, an inexpensive, easily obtained, and widely used test, holds potential evidence to be a novel biomarker in predicting CVD risk in asymptomatic individual. Prospective follow-up of ELSA-Brasil cohort is necessary to confirm the association between RDW and CVD.

A-113

Assay Development And Evaluation Of Serum Aggrecan And Versican As Novel Biomarkers For Thoracic Aortic Aneurysm And Dissection

C. Koch1, F. Cikach2, B. Willard2, S. Apte1. 1Cleveland State University, Cleveland Clinic Lerner Research Institute, Cleveland, OH, 2Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH, 3Cleveland Clinic Lerner Research Institute, Cleveland, OH

Objectives: Thoracic aortic aneurysm and dissection (TAAD) is a progressive vasculopathy with a high rate of mortality due to an increased risk of vessel wall rupture. Aorta diameter is currently the gold standard for dictating surgical intervention, however the majority of dissections occur below surgical decision limits, illustrating a pressing need for new biomarkers for aneurysm detection and dissection risk stratification. Proteoglycan accumulation in medial degeneration lesions is a histologic hallmark of TAAD. We hypothesize that the proteoglycan constituents of medial degeneration lesions will enter the circulation in aneurysm and/or dissection and can be used as diagnostic and prognostic biomarkers. The objectives of this study were to develop assays for the detection of proteoglycans and evaluate their presence in the peripheral circulation of TAAD patients.

Methods: We identified the proteoglycan constituents of the ascending aorta by tandem mass spectrometry (MS/MS) analysis of affinity-isolated proteoglycans. Ascending aorta tissue was collected from patients undergoing elective (aneurysm) or emergent (dissection) surgical intervention. Aortas from heart donors were used as normal controls. Total protein was extracted from tissue and proteoglycans isolated by anion exchange chromatography. Shotgun MS/MS was performed on isolated proteoglycans using a Thermo Scientific Orbitrap Elite hybrid analyzer. Shotgun analysis was repeated on isolated proteoglycans as well as on total aorta protein extracts using a Thermo Scientific Orbitrap Fusion Lumos tribrid analyzer to identify peptide candidates for selected reaction monitoring (SRM) assay development. Targeted analysis was performed on TAAD and control serum samples to verify candidate peptides could be identified in the peripheral circulation. Additionally, proteoglycan concentration in TAAD patient serum was determined in triplicate by a commercially available sandwich ELISA (research use only; R&D Systems). Blood from TAAD available patients (n = 25) was collected pre-operatively in 3.5 mL SST BD vacutainer tubes.

Results: The proteoglycans aggrecan and versican were identified as major constituents of medial degeneration lesions. Due to the large number of post-translational modifications in the central glycosaminoglycan domains, peptides were limited to the N- and C-terminal globular domains and included 11 and 18 unique peptides for aggrecan and versican, respectively. Two peptides for each proteoglycan were chosen for further SRM development. Targeted MS/MS analysis of TAAD serum identified peptides, but at low intensities, suggesting further pre-analytic processing, such as albumin/lg depletion, may be required. An aggrecan ELISA was optimized for serum with a sensitivity of 100 pg/mL and an intra-assay imprecision of <5.0 %CV (range: 0.0-16.5%). 11 of 25 TAAD patients had detectable aggrecan levels (≥100 pg/mL), including 3 of 5 dissection patients, with concentrations ranging from 279-17979 pg/mL.

Conclusions: Aggrecan and versican accumulate in TAAD and are detectable in the peripheral circulation by MS/MS and immunoassay. Despite consistent detection by MS/MS, serum aggrecan levels were detectable by ELISA in some, but not all cases of TAAD indicating that differences in circulating fragments may be influenced by disease progression, primary etiology, and other unknown factors. Aggrecan and versican are potential serum biomarkers for TAAD and warrant further investigation.

S38