Tuesday, August 1, 2017

Poster Session: 9:30 AM - 5:00 PM

Clinical Studies/Outcomes

A-100

Selected pro- and anti-inflammatory cytokine serum concentrations in different clinical forms of multiple sclerosis

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Background: Multiple sclerosis (MS) is an immune-mediated central nervous system disease characterized by inflammation, demyelination and axonal degeneration. The pathology of MS suggests an autoimmune cause involving cellular and humoral components of the immune system. Active MS lesions are characterized by T-cell and macrophage infiltration and the presence of immune mediators, including adhesion molecules, chemokines, and cytokines. Cytokines are proven mediators of immunological process in MS. The aim of this study was to delineate the serum cytokine profile in patients with MS and the controls and to determine in different clinical forms of MS.

Methods: This study involved 62 consecutive MS patients--28 patients with progressive MS and 34 patients with relapsing-remitting MS (RRMS). The control group consisted of 18, age and sex matched, non-immunological, neurological patients. The patients were evaluated using the Expanded Disability Status Scale (EDSS) and magnetic resonance imaging (MRI) with gadolinium. Serum samples for cytokine measurements were collected on admission. Plasma levels of proinflammatory T-helper (TH)1 (interferon (IFN)-γ) cytokines, peripheral monokines (IL-1beta, IL-6, TNF-alpha) and anti-inflammatory or down-regulatory TH2 cytokines (IL-4, IL-10) were determined by an enzyme-linked immunosorbent assay (ELISA) method.

Results: All patients with MS had significantly higher cytokine (IFN-γ, IL-1β, IL-6, TNF-α, IL-4, IL-10) concentrations compared with controls ($p < 0.001$). Increased IL-1beta, IFN-γ ($p=0.032$ and 0.041, respectively) and decreased IL-4, IL-10 ($p=0.038$ and 0.02, respectively) levels were found in progressive MS compared with RRMS. Patients with progressive MS with disease progression presented higher IL-1beta, TNF-alpha, IFN-γ and IL-10 levels than those without disease progression ($p < 0.05$). There was a significant inverse correlation between IL-10 levels and EDSS score in patients with progressive MS ($R = - 0.43$, $p < 0.05$).

Conclusion:

Profiling cytokines in multiple sclerosis may help to identify mechanisms involved in the pathogenesis of the disease, and, potentially, lead to new therapies directed at cytokines or their receptors. The level of IL-10 can serve as an additional diagnostic criterion for assessing the disability in patients with progressive MS.

A-101

Comparison of Neutrophil / Lymphocyte Ratio & Red Blood Cell Distribution Width with Cardiac Markers in Acute Coronary Syndrome

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Background: Acute coronary syndrome (ACS) is a group of symptoms for acute myocardial ischemia. The RDW (red cell distribution width), recently described as a novel risk marker, has been associated with an increased risk of cardiovascular events and routinely reported as part of the complete blood count. We assessed the relationship of hematologic parameters (RDW and NLR) with cardiac markers (Troponın I, CK-MB) in patients admitted with ACS.

Methods: In this study 228 patients were included. For all patients, a baseline blood sample was collected for routine hematological testing. The patients were diagnosed as Non ST elevation myocardial infarction (NSTEMI), ST elevation myocardial infarction (STEMI) or unstable angina (USAP) based on the elevation of cardiac troponin I levels in the first and sixth hours of admission. SPSS version 15.0 program was used for statistical analysis.

Results: There was no difference in the levels of RDW in NSTEMI and USAP groups (p=0,154). In the ACS subtypes groups, NLR showed a negative correlation with EF (p≤ 0,001)and significant positive correlation with the first hour levels of CK-MB and TnI (p≤ 0,001). It was also found that NLR showed positive correlation with STEMI groups (p≤ 0,001).

Conclusion: It was determined that there was no statistically significant difference between RDW and ACS subtypes. Finding NLR levels being significantly high in STEMI group of ACS patients revealed out that NLR can be a useful marker in ACS. We suggest that these findings should be evaluated and supported with prospective studies.

A-104

Liver Fibrosis Biomarkers and Acoustic Radiation Force Impulse Imaging for non-invasive assessment of Non-Alcoholic Steatohepatitis in patients with morbid obesity before bariatric surgery

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Background: There is a wide spectrum of liver histology in Non-Alcoholic fatty liver disease (NAFLD).Simple steatosis is generally considered benign and reversible, but steatohepatitis (NASH) can evolve to progressive fibrosis and liver cirrhosis in the long term. The early detection of NASH would make it possible to anticipate the natural course of the disease, allowing therapeutic action to be proposed before the appearance of fibrosis, therefore, identification of NASH patients is crucial. Obesity is a recognized risk factor for NAFLD. The prevalence of NAFLD in the general population ranges from 15 to 30% and increases with obesity. In overweight subjects, the prevalence of steatosis is at least two times greater than in lean subjects and in morbid obesity the prevalence of NAFLD and NASH is nearly 90% and 37% respectively. Liver biopsy is the standard for the diagnosis of NAFLD but has risks and limitations, so that non-invasive diagnostic tools such as serum biomarkers, imaging methods have been developed. The ELF test measures three markers of liver matrix metabolism in serum (hyaluronic acid, procollagen-III amino terminal peptide and tissue inhibitor of metalloproteinase-1) and the result becomes a score that indicates the level of fibrosis. Acoustic Radiation Force Impulse (ARFI) is a imaging technique that provides a quantitative measure of the tissue elasticity, shear wave velocity (SWV), that correlates with the degree of fibrosis. We aimed to develop a model that combines ELF and ARFI and to assess its feasibility for detecting NASH in morbid obese patients with suspected NAFLD.

Methods: We selected 57 morbidly obesity patients who were to undergo bariatric surgery and were classed according to their biopsy findings. Group A (n=28): normal liver or simple steatosis; Group B (n=29): NASH and/or fibrosis. All patients were evaluated with ARFI before surgery and ELF test was calculated.

Results: Significant differences in ELF and SWV results were found between the two groups (p=0.002, p=0.003). AUROC for differentiating patients of both groups using ELF and SWV were 0.780 (p=0.002) and 0.729 (p=0.003). We developed a logistic regression model that combined clinical variables, biomarkers and the SWV and defined the probability of presenting NASH and/or fibrosis (group B). The variables included were age, body mass index, metabolic syndrome, mean corpuscular volume, AST, ALT, SWV and ELF. The AUROC of the model was 0.890 (p=0.044) and was significantly higher than any of the individual variables.

Conclusion: The combination of the ELF and the Arfi represents a efficient option for the identification of obese patients with NAFLD and signs of NASH and fibrosis. Using complementary methods together with different biological bases is an advantage over the use of individual techniques and increases confidence in diagnosis. In the case of patients who are going to be subjected to bariatric surgery, the use of this model would make it possible to presurgically identify those patients with more severe hepatopathy, thus establishing a population at risk in which surgery could be prioritized, and to propose prior therapeutic actions to reduce postsurgical morbidity and mortality related to hepatopathy.

A-109

Evaluation of Glycated Albumin as a Useful Indicator for Renal Dysfunction in Diabetic and Nondiabetic Population

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Background: Glycated albumin (GA) reflects serum glucose of preceding 2-3 weeks and plays an important role in diabetes mellitus (DM). This study aimed at investigating whether GA can assess renal dysfunction in population.

Methods: 3818 individuals attending physical examination were enrolled in this cross-sectional study and divided into 5 groups: healthy subjects (n = 3238), impaired fasting glucose (n = 83), DM without renal complications (n = 317), DM with albuminuria (n = 64) and nondiabetic chronic kidney disease patients (n = 116). All analyses were conducted using the subjects with fasting venous blood and morning urine samples. Statistical analysis was done by SPSS 16.0.

Results: Among all groups, mean GA, hemoglobin A1c, fasting plasma glucose, serum creatinine were the highest and estimated glomerular filtration rate (eGFR) was the lowest in DM with albuminuria group. When eGFR was 90-105 ml/min/1.73m^2 or mildly decreased to 60-90 ml/min/1.73m^2, GA increased significantly with elevating albumin-to-creatinine ratio (ACR) from 0-10 mg/g to 10-30 mg/g to > 30 mg/g (P < 0.01 and P < 0.001). GA increased further when eGFR decreased moderately to severely as renal function continuing to deteriorate (eGFR ≤ 60 ml/min/1.73 m^2). When ACR ≤ 30 mg/g and eGFR ≤ 60 mL/min/1.73m^2, more than 50% subjects were DM patients and had significant higher GA levels than other subjects with eGFR > 105 mL/min/1.73m^2. After adjusting demographics (age at enrollment, gender and body mass index [BMI]), every 5% rise of GA levels showed a 1.778-fold increased risk in all subjects (adjusted odds ratio [OR], 1.778; 95% confidence interval [CI], 1.373-2.302; P < 0.001) and 1.737-fold risk in DM subjects (adjusted OR, 1.737; 95% CI, 1.221-2.471; P = 0.002) for occurrence of ACR > 30 mg/g in contrast to ACR ≤ 30 mg/g. Compared to eGFR > 90 mL/min/1.73m^2, 5% rise of GA levels showed a 1.482-fold risk for eGFR 60-90 mL/min/1.73m^2 (adjusted OR, 1.482; 95% CI, 1.112-1.975; P = 0.007) and 1.996-fold risk for eGFR ≤ 60 mL/min/1.73m^2 (adjusted OR, 1.996; 95% CI, 1.366-2.916; P < 0.001).

Conclusions: Increased GA serves as a risk marker for renal dysfunction and an effective complement to ACR for DM patients. GA combined with eGFR and ACR can reflect renal function changes in population, especially those DM and early diabetic kidney disease subjects whose eGFR might be in normal values.

A-111

Effects of laboratory results and lifestyle parameters on the development of non-alcoholic fatty liver disease: The Korean National Health Insurance Service-National Sample Cohort 2009-2013

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Background: The purpose of this study was to investigate the effects of anthropometric, laboratory, and lifestyle factors on the development of nonalcoholic fatty liver disease (NAFLD) in a nationwide, population-based, 4-year retrospective cohort.

Methods: The propensity score-matched study and control groups contained 1,474 subjects (940 men and 534 women) who had data in the Korean National Health Insurance Service-National Sample Cohort in 2009, 2011, and 2013. NAFLD was defined using medical records of a diagnosis confirmed by primary clinicians and meeting two previously validated fatty liver prediction models: the hepatic steatosis index and fatty liver index. Chronological changes in anthropometric variables, laboratory results, and lifestyle factors were compared to baseline values and those of the control group.

Results: Among the 5 anthropometric, 10 laboratory, and 3 lifestyle factors, chronological change in no single variable appeared to be statistically associated with NAFLD development in either men or women. Interestingly, baseline characteristics before the diagnosis of NAFLD seemed to be important regardless of time-dependent change throughout the 4-year period. Nevertheless, triglycerides showed prominent decrease in men during the period of NAFLD development, while weight and exercise changes were noticeable in women.

Conclusion: Although baseline characteristics might be important in NAFLD development, chronological changes in anthropometric, laboratory, and lifestyle factors are insufficient to predict development of NAFLD. However, we propose that early screening strategies for NAFLD should be strongly recommended for people with abrupt chronological changes in specific parameters, especially waist circumference and exercise degree for women and serum triglycerides level for men.

A-112

PREVALENCE OF METABOLIC SYNDROME IN GRANITE WORKERS

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BACKGROUND: The prevalence of the metabolic syndrome (MS) has significantly increased over the last few decades and has become a main health challenge worldwide. Prevalence of MS is quickly rising in developing countries due to changing lifestyle. It was considered worthwhile to study MS and its components in granite workers since granite factories are situated in and around Khammam area. Moreover, no studies of MS in granite workers have been reported in literature. **OBJECTIVES:** Aim of our study is to assess the prevalence of metabolic syndrome and its components in granite workers. **MATERIALS AND METHODS:** 210 male workers in the age group of 20-50 working in granite industries located in and around the Khammam town of Telangana State are selected for the present study. Blood pressures (BP), waist circumference (WC) were measured. Fasting blood samples were collected for the estimation of glucose and lipids. **RESULTS:** 69 subjects out of 210 were identified as having MS based on updated National cholesterol education program- Adult Treatment Panel III (NCEP-ATP III) guidelines. **CONCLUSION:** MS should be identified and remedial measures may be suggested, so that the risk of hypertension, cardiovascular risk, diabetes and the resultant morbidity is minimized and can be delayed.

Prevalence of MS and its components		
Paramaters	No Of Granite Workers	Percentage
Elevate BP	85	49
Elevate waist Circimference	61	29
Elevated TG	52	25
Reduced HDL	72	34
Elevated Glucose	42	20
Metabolic Syndrome	69	33

A-113

Evaluating neonatal minimum volumes with Abbott Architect c8000 and Sysmex XN

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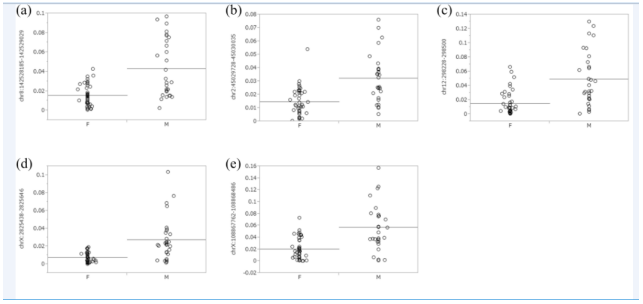
Background: Our neonatologists approached the laboratory to find a solution to reduce neonatal blood collection volumes. Nurses draw specimens in wide bore BD Microtainers (Cat # BD 365967) which can potentially reduce the amount of blood drawn from neonates, but short collections lead to high rates of QNS and redraws. Nurses frequently collected whole blood in spun hematocrit tubes and phase platelet devices in situations of previous QNS or other collection issues. We wanted a solution that was efficient and productive for both nursing and the laboratory that would maximize quality and safety for the neonates.**Methods:**We started by reviewing actual patient hematocrit values to assess the number (%) of high/low hematocrit specimens. 155 specimens in one month showed 87% of neonates with a hematocrit ≤50 and 60% of neonates ≤40. Based on this population, we conservatively based the study on a hematocrit of approximately 60% to establish extreme minimum volumes. We selected 20 most frequently ordered chemistry tests and included the volume necessary for HIL (Hemolysis, Icterus, and Lipemic specimen integrity testing.) Hematology focus was on replacing the manual parameters spun hematocrit (0.225 mL) and phase platelets (0.020 mL) with automated testing.

Results: The Abbott Architect c8000 Sampling Dead Volume + Over Aspiration Volume (DV/OAV) is 0.058 mL. This DV/OAV plus the accumulative aspiration volumes (calculated from the Abbott Architect Sample volumes) ranges from 0.083 mL (minimum 4 assay panel + HIL) to 0.1337 mL (maximum 20 assay panel plus

HIL). Whole blood was adjusted to resemble elevated neonate hematocrits at >60%, centrifuged and transferred to Evergreen Scientific sample cups placed in standard aliquot tubes by plastic transfer pipette. We determined the following recovery volumes of plasma after centrifugation: 0.200 mL whole blood yielded 0.076 mL plasma; 0.300 mL whole blood yielded 0.114 mL plasma; 0.400 mL whole blood yielded 0.152 mL plasma. The Abbott Architect instrument dead volume is 0.058 mL. Using similarly adjusted specimens (hematocrits at >60%), we performed volume trials on Sysmex XN for determination of a repeatable minimum volume that produces 22 parameters. We demonstrated that 0.150 mL is required for an automated panel including WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW-CV, PLT, MPV, NRBC, IPF, and automated differential plus adequate volume to make a slide. This reduced the specimen volume from of 0.245 mL (2 manual tests) to 0.150mL while optimizing the availability of test options and improved quality. A visual chart of testing volumes and specimen requirements was created for NICU nurses with color photos as guides.

Conclusion: Abbott Architect c8000 instrument can perform 10 tests with initial volume of 0.3 mL whole blood and 20 tests on 0.4 mL whole blood (prior to centrifugation). Sysmex XN can perform CBC with platelets and a slide can be made with 0.150 mL whole blood. This project resulted in significant reduction of specimen volume collected, reduced manual processes, and promoted reliable chemistry and hematology testing to clinicians in caring for our most tiny and vulnerable patients. Satisfaction among our NICU partners has been enormous.



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Growth Differentiation Factor-15 is a New Biomarker with Independent Prognostic Significance for Survival and Renal Outcomes in Different Cohorts of Patients with Light Chain (AL) Amyloidosis

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Background: Growth differentiation factor-15 (GDF-15), a member of TGF-beta family, is involved in several pathological conditions, which include inflammation, cancer, cardiovascular, pulmonary and renal diseases. Serum GDF-15 levels add prognostic information to conventional prognostic factors, such as NT-proBNP and troponins, in cardiovascular disorders and also have shown to be associated with renal damage and risk of end stage renal disease in patients with diabetes. Based on the above data, we evaluated the prognostic value of GDF-15 levels in patients with AL amyloidosis and showed that in a cohort of 77 patients GDF-15 was associated with early death, shorter survival and progression to dialysis, independently of the cardiac biomarkers and renal stage. In order to validate the prognostic value of serum levels of GDF-15, we evaluated GDF-15 in two independent cohorts of patients treated in two different centers (Pavia Amyloidosis Center and Department of Clinical Therapeutics, Athens). **Methods**: Circulating levels of GDF-15 were measured by a novel pre-commercial immunoassay (Roche Diagnostics), along with measurements hs-Troponin-T and NT-proBNP in more than 800 serial stored samples using electrochemiluminescence techniques. The Pavia cohort included 202 and the Athens cohort included 107 patients with AL amyloidosis. Standard criteria were used for the diagnosis, evaluation of organ involvement and cardiobiomarker-based risk stratification. Renal staging was based on baseline proteinuria >5g/day and eGFR<50ml/min. Median age and involved FLC levels were similar between the two cohorts but there were differences in other baseline characteristics including heart involvement and Mayo stage Median follow up for the Pavia cohort was 18-months and for the Athens cohort was 45-months (p<0.001), while survival at 2 years was identical. **Results**: Median GDF-15 levels was 3,027pg/ml in Pavia (range 624->100,000pg/ml) and 3,854pg/ml (range 626-71,475pg/ml) in Athens cohort (p=0.09); the upper quartile of GDF-15 levels however was ≥5,658pg/ml for the Pavia and ≥7,553pg/ml for Athens cohort, while 90% and 94% of patients in the two cohorts had GDF-15 levels >1,200pg/ml (the upper limit of normal for individuals without cardiovascular disease). We then evaluated the prognostic significance of GDF-15 levels in the two cohorts by applying the previously identified cutoff of 7,575pg/ml. GDF-15 above cutoff was associated with significantly shorter survival both in Pavia (17 months vs not reached, p=0.003) and in Athens cohort (13 vs 47 months, p=0.03). We then evaluated the prognostic significance regarding renal outcomes (dialysis): GDF-15 >4,000pg/ml was associated with a HR of 6 (95% CI 2015.6, p=0.001) in Athens cohort (progression to dialysis within 2 years in 7% vs 47%); however, very few events have occurred in Pavia cohort and analysis was inconclusive. Although renal stage discriminated 3-groups in univariate analysis (p=0.03), in multivariate analysis, GDF-15 >4,000pg/ml outperformed renal stage and was the only independent prognostic factor for dialysis risk. **Conclusion**: This study validated and confirmed in two independent cohorts, with differences in their characteristics, the prognostic value of GDF-15, which emerges as a novel biomarker with prognostic implications for different outcomes in patients with AL amyloidosis. Importantly, GDF-15 emerges also as new biomarker for renal outcomes in patients with AL-amyloidosis.

A-118

Prostate-Specific Antigen (PSA) Screening Rates in the United States, 2010-2015: Implications for Practice Interventions

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Background: Prostate-specific antigen (PSA) is the most commonly used cancer screening test in men. U.S. Preventive Services Task Force (USPSTF) recommended against PSA screening of all men regardless of age in 2012. This recommendation is endorsed by both American Academy of Family Physicians and American College of Preventive Medicine. By 2013, other medical organizations (e.g., American Cancer Society, American Urological Association and American College of Physicians), had recommended offering PSA screening to men between 50 and 69 years of age and with at least 10 years of remaining life expectancy, but only after a process of informed and shared decision making. The objective of this study was to evaluate the rate of PSA screening and its trend in different age groups from 2010 through 2015 using large databases covering approximately one-third of all privately insured men in the U.S. plus all men insured by Medicare. Analyzed data are expected to provide information on gaps in clinical practice, thus informing interventions needed to promote good laboratory screening practices.

Methods: Claims data for men under 65 years of age were collected using Truven Health Analytics' MarketScan database for commercial claims and encounters in 2010-2015 (9.9-16.6 million men). For men aged 65 years or older, claims data for the entire Medicare-insured population were evaluated using CMS' virtual research data center encompassing 17.7-21.8 million men for these years. A two-sided Poisson regression was used to determine P for trend, calling $P < 0.05/n$ as significant, where n is the number of groups analyzed (Bonferroni correction). To consider PSA testing for screening only, all claims with any one or more of 62 prostate or urinary conditions implying use of testing for purposes other than screening were deleted.

Results: PSA-based screening rates in 2010-2015 were: 2% in men age 30-39, 5%-6% in men age 40-49, 29%-31% in men age 50-59, 33%-36% in men age 60-64, 9%-12% in men age 65-69, 11%-14% in men age 70-74, and 6%-9% in men older than 74. There were no significant temporal trends in men aged 30-39 years ($P = 0.18$), 50-59 years ($P = 0.08$), 65-69 years ($P = 0.16$), 70-74 years ($P = 0.05$) and older than 74 years ($P = 0.16$). There were significant downward trends in men aged 40-49 years ($P = 0.005$) and 60-64 years ($P = 0.003$). For all age groups, PSA screening rate decreased from 2010 to 2015 by 1%, 6%, 2%, 6%, 9%, 13% and 10%, respectively, for men aged 30-39, 40-49, 50-59, 60-64, 65-69, 70-74 and

greater than 74 years (1%-13% decrease in PSA screening rate for the 7 age cohorts).

Conclusion: All medical organizations recommended against PSA screening of men older than 69 and younger than 50 soon after the earlier recommendation by the USPSTF in 2008, but there are still a substantial proportion of younger (2%-6%) and older (6%-14%) men who are screened with PSA, contrary to all existing practice guidelines. Further research is needed to understand the reasons for overuse of PSA screening in order to identify more effective means to prevent overuse.

A-119

The dibucaine number is required to accurately predict pseudocholinesterase phenotypes

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OBJECTIVE: The relationship between pseudocholinesterase (PChE) phenotypes and dibucaine numbers (DNs) is used to identify individuals who may experience prolonged effects of neuromuscular-blocking general anesthetics administered during surgery (Table 1). **The objective of this study is to determine if uninhibited or dibucaine-inhibited PChE activity sufficiently predicts enzyme phenotype.**

METHODS: Pairs of uninhibited and dibucaine-inhibited PChE activity data were analyzed for 39,719 patient samples across 43 laboratories. DNs were calculated for each sample from this paired data (Equation 1). The uninhibited and dibucaine-inhibited PChE activity of each sample was then evaluated relative to its corresponding DN to determine if a correlation exists between enzyme activity and DN.

Equation 1 DN=100*(1-PChEDi activity/PChE activity)

RESULTS: Wild-type, heterozygous, and homozygous atypical PChE phenotypes were present in the data set as indicated by the DN calculation (Table 1).

Table 1

DN	PChE Phenotype	Recovery from general anesthesia	Frequency - this study
DN>72	Wild-type (E^u_1 E^u_1)	Normal	94.2% (34,565)
35≤DN≤72	Heterozygous atypical (E^u_1 E^a_1)	Prolonged	5.6% (2083)
DN<35	Homozygous atypical (E^a_1 E^a_1)		0.2% (71)

Consistent with literature, over 90% of PChE samples in this study were wild-type (DN>72) and less than 0.5% were homozygous atypical (DN<35). 100% of uninhibited homozygous atypical PChE samples displayed activity <18,000 U/L, as did 97.1% of uninhibited heterozygous, and 98.5% of uninhibited wild-type samples. Despite the small fraction of heterozygous and wild-type samples with uninhibited PChE activity >18,000 U/L, there was no overall correlation between uninhibited activity and phenotype or DN.

Dibucaine-inhibited PChE activity for all phenotypes did not exceed 16,000 U/L and did not correlate with phenotype or DN.

CONCLUSIONS: The DN calculation is essential for accurate PChE phenotyping. Taken in isolation, neither uninhibited nor dibucaine-inhibited PChE activity correlates with enzyme phenotype.

These data may be used to determine the DN for a patient receiving general anesthesia if they have previously suffered a prolonged recovery from anesthesia or have a family history of atypical phenotypes. Application of DN to management of these patients may prevent unexpected postoperative respiratory muscle paralysis that lasts hours to days and necessitates mechanical ventilation.

A-120

An observational prospective single center study to assess utility of serum cystatin C and its estimated GFR among various subgroups of patients- an experience in semi urban locality

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Background: Serum creatinine and cystatin C are complementary markers of GFR. Whereas serum creatinine is affected by age, race, sex and muscle mass, cystatin C remains unaffected. Cystatin C has been used extensively as a research tool but it is not commonly done in routine laboratories in India because of its cost. Study aims to assess the subgroups of patients with nephropathy who get additional benefit from cystatin c test over creatinine. **Methods:** Inclusion criteria- Consecutive 131 subjects seen and referred by nephrologist and physician.Exclusion criteria- Patients with age greater than 75 years, those suffering from hypo or hyperthyroidism, patients taking steroids.1) Normal male: 20 normal female: 20 (forcomparison). 2)Hypertensive patients (s. creatinine: >1.5mg/dl in males, >1.3 mg/dl in females): 21 3)Chronic glomerulonephritis (urine protein +++): 15. 4)Diabetic nephropathy (s. creatinine >1.5mg/dl in males, >1.3 mg/dl in females) : 55.

We estimated s. creatinine and urine creatinine by Jaffe kinetic. Cystatin c estimated by by turbidimetry method. Microalbumin done by turbidimetry method (Agappe India) Urine protein done by suphosalicylic turbidimetry method. Tests done on semiautomated instrument. EGFR estimation from creatinine calculated by Cockcroft-Gault equation, and from cystatin C by Hoek formula GFR = -4.32+ (80.35 × 1/cystatin C (mg/l).

Results: We report good correlation in healthy male & female subjects between values of creatinine, cystatin C, GFR estimated from the above and albumin/ creatinine Ratio. Reference range of cystatin c: (male) 0.78 to 1.2 mg/l, (female) 0.4 mg to 0.8 mg/l . Out of 21 Hypertensives patients (mean age 50 years), mean for creatinine eGFR was 52±18 ml with 4 patients in mild/stage 2 and rest 17 in moderate/stage 3 whereas cystatin C eGFR was reported mean of 83ml ±40ml with 2 patients in mild reduction, 8 in moderate reduction and 11 patients within normal range. Therefore only 50% of hypertensive patients showed eGFR values in abnormal range with cystatin C as compared to creatinine as verified by normal urine microalbumin. This variation in creatinine results might be due to above mentioned factors. Out of 15 patients of glomerulonephritis mean for age was 41±15 years. About 40% of these patients had borderline creatinine values (mean 1.64 mg/dl) while all cystatin C values are in pathological range (mean 2.5 mg/dl). In 55 patients suffering from diabetic nephropathy, all values show good correlation between creatinine and cystatin C. Mean for creatinine was 2.21±0.9 mg/dl with eGFR with 37±24 ml; mean for Cystatin c was 2.19±1.29 mg/L with eGFR 37.2±25 ml. All the above patients had albuminuria.**Conclusion:**Above results show the importance of cystatin C and its eGFR in hypertensives and patients suffering from glomerulonephritis. It can be used as a complementary test in patients suffering from diabetic nephropathy.

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Graft-derived cell-free DNA - a promising rejection marker in cardiac transplantation - Results from a prospective observational trial

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Background: Reliable noninvasive markers for early detection of rejection after heart transplantation are lacking. Immunosuppressant therapeutic drug monitoring is more useful to prevent toxicity rather than to predict efficacy. Graft-derived cell-free DNA (GcfDNA) has shown promise as a biomarker for the early detection of graft injury.

Methods: In a prospective observational trial, GcfDNA was monitored in 84 adult cardiac transplant recipients followed over at least one year post transplantation. cfDNA was extracted from >1 ml EDTA plasma, obtained in cell-free DNA BCT tubes. GcfDNA was determined as described elsewhere (Clin Chem 2013; 59: 1732-1741). The turnaround time for an initial sample is about 2 days and one working day for any consecutive sample. Biopsies were done upon clinical suspicion of acute rejection and compared to GcfDNA test results.

Results: GcfDNA percentage was highly elevated (>5% of total cfDNA) on the first day after transplantation, evaluated in a subset of 15 patients, presumably due to ischemia/reperfusion damage. The median GcfDNA percentage decreased in stable patients with no signs of graft injury within the first week to a baseline value <0.25%, where it remained throughout the one year observation period. In 19 patients with samples drawn during biopsy-proven acute rejection periods (n=25), values were about 5-fold higher (median: 0.51%, 95%-CI 0.42-0.87%) than median values observed in samples (n=208) from 67 stable patients without rejection (median: 0.10%, 95%-CI 0.08-0.12%). In comparison to 23 patients with negative biopsy (n=23 samples; median: 0.19%, 95%-CI 0.16-0.26%), the median observed in patients with biopsy-proven rejection was 2.7-fold. In 14 otherwise clinically stable patients with samples available 9 to 30 days prior to diagnosis of biopsy-proven acute rejection (n=22), 5-fold elevated GcfDNA values (median: 0.47%, 95%-CI 0.26-0.61%) compared to stable patient samples were observed. hsTroponinI showed only a moderate correlation with GcfDNA (Spearman correlation coefficient (R): 0.51, 95%-CI 0.40-0.60, n=222).

Conclusion: Plasma GcfDNA determinations allowed for early detection of cardiac transplant patients with acute rejection and may be helpful to personalize post-HTx immunosuppression.

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The Application of EFIRM technology in ALDH2 rs671 Genotyping

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Background: Mitochondrial aldehyde dehydrogenase-2 (ALDH2) is an enzyme that oxidizes acetaldehyde into acetic acid in the alcohol metabolism. The enzyme also catalyzes vascular bioactivation of the antianginal drug nitroglycerin. As a dominant negative inhibitor, Glu504Lys (also named rs671) variant significantly reducesthe enzyme activity in heterozygotes and abolishesthe activity in homozygotes. The variant, which commonly occurs in East Asian populations, has been reported to relatewith many different kinds of disorderssuch as alcohol liver disease, colorectal cancer, and esophageal cancer. Based on our novel core technology-electric field induced release and measurement (EFIRM), EZlife Bio. has developed an effective, accurate and inexpensive genotyping method to detect the mutants of ALDH2.

Methods: EFIRM is an electrochemical technique that can rapidly and efficiently capture DNA targets in the fluid environment. EFIRM method has a number of key characteristics: 1. A large amount of the specific DNA probes (for ALDH2 mutants) can be efficiently immobilized to the surface of an electrode through the unique conducing polymer. The immobilized DNA probes are so sensitive to detect a single base pair mutation in the gene. 2. After this immobilization occurs, the PCR amplified ALDH2 fragments are added to the surface of the electrode and pulsed electric fields are used to drive the hybridization process between the probes and the target DNA (ALDH2 DNA fragment).And the signals are quantified using an enzymatic readout process. 3. A high-throughput array of electrodes allows 96 different samples to be simultaneously assayed using the EFIRM method.

Results: We collected 19 humans' buccal epithelial cells, and extracted genomic DNAs from each samples. Those DNA samples were further amplified by polymerase chain reaction (PCR). The PCR products amplified with different primers were used for genotyping by EFIRM *versus* Sanger sequencing method as a control.The EFIRM testing results of all the 119 samples including 4 mutant homozygote and 35 heterozygotes were 100% concordant to the data obtained from Sanger sequencing. The used amount of genomic DNA for PCR assay was in the range of 0.2-20 ng.

Conclusion: Our data indicate that EFIRM is effective, accurate, rapid, user-friendly, and cost effective method for the genotyping of ALDH2 rs671.

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Multicenter Evaluation of Imipenem MIC Results for Gram Negative Bacilli Using MicroScan Dried Gram Negative MIC Panels

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Background: A multicenter study was performed to evaluate the accuracy of reformulated imipenem on a MicroScan Dried Gram Negative MIC (MSDGN) Panel when compared to frozen CLSI broth microdilution reference panels.

Materials/Methods: For efficacy, MSDGN panels were evaluated at four sites by comparing MICs obtained using the MicroScan panel to MICs using a CLSI broth microdilution reference panel. A total of 419 gram-negative bacilli clinical isolates (39 *Acinetobacter* species, 295 *Enterobacteriaceae*, and 85 *Pseudomonas aeruginosa*) were tested using the turbidity and Prompt™* methods of inoculation. For reproducibility, a subset of 10 organisms was tested on MSDGN panels at each site. MSDGN panels were incubated at 35 ±2ºC and read on the WalkAway System, the autoSCAN-4 instrument, and read visually. Read times for the MSDGN panels were at 16-20 hours. Frozen reference panels were prepared and read according to CLSI/ISO methodology. FDA breakpoints (µg/mL) used for interpretation of MIC results were: *Acinetobacter* spp. ≤ 2 S, 4 I and ≥ 8 R; *Enterobacteriaceae* ≤ 1 S, 2 I, ≥ 4 R; *Pseudomonas aeruginosa* ≤ 2 S, 4 I, ≥ 8 R.

Results: When compared to frozen reference panel results, essential and categorical agreements for isolates tested in Efficacy are as follows:

Read Method	Essential Agreement %		Categorical Agreement %		Very Major Errors %		Major Errors %		Minor Errors %	
	T	P	T	P	T	P	T	P	T	P
Visual	98.3 (412/419)	97.4 (408/419)	92.4 (387/419)	93.6 (392/419)	0.0 (0/61)	0.0 (0/61)	0.9 (3/332)	0.3 (1/332)	6.9 (29/419)	6.2 (26/419)
WalkAway	97.9 (410/419)	96.4 (404/419)	91.6 (384/419)	92.4 (387/419)	0.0 (0/61)	0.0 (0/61)	0.9 (3/332)	0.6 (2/332)	7.6 (32/419)	7.2 (30/419)
autoSCAN-4	98.3 (412/419)	96.7 (405/419)	93.1 (390/419)	93.6 (392/419)	0.0 (0/61)	1.6 (1/61)	0.9 (3/332)	0.6 (2/332)	6.2 (26/419)	5.7 (24/419)
T = Turbidity inoculation method, P = Prompt* inoculation method										

Reproducibility among the four sites was greater than 95% for all read methods for both the turbidity and Prompt* inoculation methods.

Conclusion: This multicenter study showed that reformulated imipenem MIC results for gram-negative bacilli obtained with the MSDGN panel correlate well with MICs obtained using frozen reference panels.

†Deceased 29 November 2016.

* PROMPT is a registered trademark of 3M.

Pending clearance by US FDA, CE compliance, and other regulatory registrations.

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Evaluation of the Bio-Rad D-100™ HemoglobinTesting System

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Background: The D-100 is a high throughput automated test system used to quantify hemoglobin A1c (A1c) in whole blood samples. The D-100 uses High Performance Liquid Chromatography (HPLC) to separate hemoglobin fractions and obtain an HbA1c result that is expressed in NGSP or IFCC units. The D-100 also utilizes a bi-directional LIS interface and offers the capability of automatically reviewing (flagging or releasing) the A1c results on the system.

Objective: The purpose of this study is to verify and validate the manufacturer claims of 10,000 tests (injections) per analytical cartridge with prefilter change every 2,000 tests on a single calibration. This testing included precision and accuracy checks, sample throughput, hemoglobin variant detection with no interference from heterozygous hemoglobins S, C, D and E, and workflow studies.

Methods: Beginning January 4, 2017 a new analytical cartridge and prefilter were installed on a D-100. Calibration and QC were run per guidelines. During the 10,000 test sample run study, 4 patient EDTA whole blood samples at ~ 5, 6.5, 8 and 12 % A1c were selected and run as precision samples in duplicates, twice a day for 10 days. Additionally, 40 samples whose NGSP values were pre-assigned by SRL (Secondary Research Laboratory) were run in duplicates along with a linearity kit and 2 levels of diabetes controls. The A1c values from D-100 were compared to the NGSP values. Workflow timing was evaluated on 2 separate daily runs from start to finish. Hemoglobin variants were compared to gel electrophoresis.

Results: The analytical cartridge performed flawlessly over 30 days for 10,000 tests without recalibration, loss of precision or abnormal chromatography. Total precision calculations for the 4 precision samples were 0.86, 0.73, 0.87, and 0.86%. The sample throughput was confirmed to be 45 seconds per sample. The "Time to first result" was confirmed to be 2 minutes 15 seconds, where the 45 second assay of the first sample in the run follows a 1 minute 30 second system flush. Each successive sample of the run is 45 seconds.

Conclusion: The performance of the Bio-Rad D-100 met all of the manufacturers stated claims. The D-100 saves >80% in tech time over our previous system, the Bio-Rad VARIANT™ II TURBO. With the built-in result review criteria and the bi-directional LIS interface, >90% of our patient samples are run and verified with no tech intervention.

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Liver injury and endotoxemia in male and female alcohol-dependent individuals admitted to an alcohol treatment program

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Background: Interactions between the liver, the gut, and the immune system are critical components of alcoholic liver disease (ALD). The aim of this study was to explore the associations between alcohol-induced liver injury, endotoxemia, and inflammation at admission and over time during abstinence; and to examine the sex-related differences in these parameters in alcohol-dependent individuals admitted to an alcohol treatment program. **Methods**: A cohort of 48 otherwise healthy participants with alcohol use disorder, but no clinical signs of alcoholic liver injury (34 males (M)/14 females (F)) admitted to an alcohol detoxification program, was stratified into two groups based on baseline plasma ALT levels (as a marker of liver injury). Group 1 (ALT < 40 U/L, 7M/8F) and Group 2 (ALT ≥ 40 U/L, 27M/6F) were identified. Plasma biomarkers of liver damage, endotoxemia and inflammation were examined at baseline (T1), day 8 (T2) and day 15 (T3) of the admission. The drinking history was also evaluated. **Results**: Sixty-nine percent of patients had elevated markers of liver damage, including ALT (98.55±9.82 *vs* 26.47±2.28 U/L), AST (130.7±17.49 *vs* 34.53 ±5.18 U/L), and cytokeratin 18 (CK18) M65 and M30 (890.3±164.6 *vs* 308.1±105.9 U/L and 378.2±59.6 *vs* 241.6±36.1 U/L, respectively; Group 2 *vs* Group 1) at baseline, indicating the presence of mild ALD. Elevated CK18 M65:M30 ratio suggested a greater contribution of necrotic rather than apoptotic hepatocyte cell death in the liver injury observed in these individuals. Positive correlations were observed in Group 2 at T1 between both CK18 M65 and ALT ($r = 0.473$, $p = 0.005$) and CK18 M30 and ALT ($r = 0.357$, $p = 0.041$). CK18 M30 was positively correlated with average drinks per drinking day at T1 in males ($r = 0.503$, $p = 0.007$). Females showed greater elevations of liver injury markers compared to males (e.g., ALT 136.2±43.8 *vs* 90.19±6.9 U/L), although they had fewer drinks per day (10.5±1.9 *vs* 15.1±1.0) and shorter lifetime duration of heavy drinking (11.5±3.6 *vs* 18.9±1.9). Liver injury was associated with systemic inflammation, specifically, elevated plasma TNF-α levels. Compared to patients without liver injury, patients with mild ALD had greater endotoxemia (increased serum LPS levels), which decreased with abstinence and this decrease preceded the drop in CK18 M65 levels. A positive correlation between LPS and ALT levels was observed at T1 only in Group 2 males ($r = 0.404$, $p = 0.037$). **Conclusions**: The study documented the association of mild alcohol-induced liver injury and endotoxemia, which improved with two weeks of abstinence, in a subset of alcohol-dependent individuals. Females demonstrated higher levels of biomarkers of liver injury compared to males, although they had lower daily alcohol intake and shorter lifetime duration of heavy drinking

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Investigated Genotype and Phylogenetic Relationship of Carbapenem-Resistant *Enterobacteriaceae* in Regional Hospital in Taiwan from 2011 to 2016

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Background: *Enterobacteriaceae* are inhabitants of the intestinal flora and are among the most common human pathogens, causing infections such as cystitis and pyelonephritis with fever, septicemia, pneumonia, and meningitis. Carbapenems are important last-line β-lactams antibiotics for treatment of multi-drug resistant *Enterobacteriaceae*. Carbapenem-resistant *Enterobacteriaceae* (CRE) are difficult to treat because they confer on the bacteria which resistant to most of β-lactams antibiotics which may result in global health problems. Therefore, the monitoring of CRE becomes an important issue in the clinical workplace. CRE have been reported worldwide as a consequence largely of acquisition of carbapenemase genes. In this study, we investigated the presence of carbapenemase genes expression and then follow the data to analyzed homology of *Enterobacteriaceae* with carbapenem resistance.

Methods: According to Clinical and Laboratory Standards Institute (CLSI) guidelines (M100-S21), the clinical specimens collected from August 2011 to July 2016 were tested for drug susceptibility to imipenem, meropenem and ertapenem using disk diffusion method. Polymerase chain reaction (PCR) was using specific primers to detect beta-lactamase (bla) genes (KPC-2, NDM-1, IMP and VIM). Pulse-filed gel electrophoresis (PFGE) was analyzed genetic relationship among isolates using restriction enzyme *Xba*I.

Results: The 255 CREs clinical specimens were isolated and analyzed from En Chu Kong hospital of Taiwan (with 498 beds of teaching hospital). Among those bacterial strains, the most common species were *Klebsiella pneumoniae* (n=149), followed by *Escherichia coli* (n=32), *Morganella morganii* (n=24), and other species (n=50). Of which, fourteen isolates contained KPC-2 gene (13 *K. pneumoniae* and 1 *E. coli*), nine strains detected to contain IMP gene (4 *K. pneumoniae*, 2 *E. hermannii*, 2 *Enterobacter cloacae*, and 1 *Citrobacter freundii*), one strain expressed VIM (*E. aerogenes*) and found two NDM-1 positive strain (*E. aerogenes* and *E. coli*). For this data in Taiwan, we first reported presence of NDM-1 and VIM in *E. aerogenes*. PFGE analysis found >90% belonging to same pulsotype for bla_{KPC-2}-carrying *K. pneumoniae* isolates that displayed high level correlation of antibiotic resistant strains. However, the 4 IMP-positive *K. pneumoniae* no major pulsotype was found.

Conclusion: Our results showed that the prevalence of carbapenemase genes in CREs was 10.2%. Among 255 CREs, 229 were carbapenem-resistant did not presence carbapenemase gene, and we speculated that those strains might harbor other carbapenemase genes or resistance mechanisms (ex: decreased expression of outer membrane protein). In the future work, we could use multiplex PCR or reverse transcription PCR continuous surveillance and investigation of carbapenem-resistant isolates to understand carbapenem-resistant mechanisms. In conclusion, this study indicated CRE with bla_{KPC-2} was mainly in *K. pneumoniae* with high level phylogenetic relationship in our hospital. Hence, we should establish the appropriate infection control policies to prevent spread of potential resistant strains for patients' healthcare to avoid the nosocomial transmission and cluster infection.

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Decrease of Urotensin-II Activity in Women with Restless Legs Syndrome

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Background

Restless legs syndrome (RLS) is a chronic sensorimotor disorder characterized by an irresistible urge to move the legs. The pathophysiological mechanism of RLS has not been completely elucidated. This study was undertaken to compare the levels of urotensin II, a vasoactive peptide, in patients with restless legs syndrome and healthy controls and to examine possible roles of urotensin in the development of restless legs syndrome.

Patients and Methods

A total of 64 female patients and 53 age- and body mass index-matched healthy female controls were included. Patients with conditions known to influence the vascular tonus such as hypertension, diabetes, or vascular diseases were excluded. The diagnosis of RLS was based on the International RLS Working Group criteria and all patients met the four essential diagnostic criteria required to establish a diagnosis of RLS.

International Restless Legs Syndrome Study Group (IRLSSG) which is an assessment tool directing questions on the typical symptoms of RLS using a 5-point scale (i.e. between 0 and 4). A total score of 0 to 10, 11 to 20, 21 to 30, and 31 to 40 is indicative of mild, moderate, severe, and very severe RLS, respectively .Also the severity of RLS was assessed using John Hopkins Restless Legs Severity Scale (severity score 1=mild ,2= middle ,3= severe). The two groups were compared with respect to demographic data, routine blood tests, complete blood count parameters, and Urotensin II levels.

Results

Average serum Urotensin II levels were significantly lower among restless legs syndrome patients than among controls (1.43±0.46 and 1.94±0.67, respectively). A significant negative correlation with increasing disease severity scores and Urotensin II levels was found ($p=0.001$, $r = -301$) . Diastolic and systolic blood pressure values were normal in both groups with no significant differences (Table 1) . On the other hand restless legs syndrome patients had significantly lower Hb, MCV, and MCH ($p=0.014$, $p=0.015$, $p=0.04$, respectively). No correlations between Urotensin II and CRP, ESR, glucose, HbA1c, vitamin B12, folic acid, albumin, total protein, and calcium were found.

Conclusion

RLS is a disease of unknown etiology. Since a proposed mechanism for the development of RLS involves the alterations of the peripheral vascular tone, we decided to examine the association between RLS and urotensin, which is a neuropeptide with known effects on the vascular tone. Our results suggest that urotensin may have a role in the pathophysiology of RLS both through vascular mechanisms and also through

its effects on the central nervous system. Further clinical multi-center studies may shed more light on potential therapeutic modalities that take this hypothesis into consideration.

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Evaluation of the Stratus CS Acute Care Diagnostic System and ADVIA Centaur XP Immunoassay System for Cardiac Troponin I

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Objective: The objective of this study was to demonstrate diagnostic equivalence between the cardiac troponin I (cTnI) method on the point-of-care Stratus® CS Acute Care™ Diagnostic System and the laboratory-based ADVIA Centaur® TnI-Ultra™ assay on the ADVIA Centaur XP Immunoassay System (both from Siemens Healthcare Diagnostics Inc.) in the determination of myocardial infarction (MI).

Relevance: Troponin is recognized as the preferred biomarker in detection of MI given its high clinical sensitivity and myocardial tissue specificity. The Third Universal Definition of MI, endorsed by national societies of cardiology and heart foundations, requires at least one cTnI value above the 99th percentile upper reference limit (URL) for detection of MI. The Stratus CS and ADVIA Centaur XP systems display optimal precision at their 99th percentile URL with a CV≤10%, allowing reliable detection of changing cTnI values.

Methodology: A comparison study was performed on the Stratus CS and ADVIA Centaur XP systems using frozen plasma samples from 110 patients suspected of having MI at two time points per patient. Patients were categorized as positive or negative for MI based on the presence or absence of at least one elevated cTnI value for each platform relative to the URL. Final diagnosis according to the Third Universal Definition of MI was provided for each patient as the reference standard for comparison.

Validation: Contingency tables were generated comparing patient outcome as determined by each system to the reference standard. The 99th percentile URL for MI is 0.07ng/mL for the Stratus CS System and 0.04ng/mL for the ADVIA Centaur XP System. Comparative receiver operating characteristic (ROC) curves were generated for each time point.

Conclusion: Clinical concordance was demonstrated between the Stratus CS System and ADVIA Centaur XP Immunoassay System for troponin I.

Table 1. Diagnostic performance measures for cTnI on Stratus CS and ADVIA Centaur XP systems.

Estimate	ADVIA Centaur XP System	Stratus CS System
Sensitivity, 95% confidence interval (%)	100.0 (92.9–100.0)	95.9 (86.3–98.9)
Specificity, 95% confidence interval (%)	100.0 (94.0–100.0)	100.0 (93.8–100.0)
Positive predictive value (%)	100.0	100.0
Negative predictive value (%)	100.0	96.7
Draw 1 area under the curve, 95% confidence interval	0.947 (0.902–0.991)	0.865 (0.801–0.929)
Draw 2 area under the curve, 95% confidence interval	1.00 (1.00–1.00)	0.99 (0.97–1.00)

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The use of procalcitonin as a sepsis marker in a community hospital

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Background: Procalcitonin is a biomarker that shows good sensitivity and specificity in identifying septic patients. This study investigated the diagnostic accuracy of procalcitonin in a community hospital setting and how it compared to lactic acid. It also explored the impact on patient care pre and post implementation of procalcitonin in regards to direct costs and length of stay.**Methods:** There were two methods used for this study. First, two comparative groups were analyzed using an exploratory descriptive case-control study with secondary analysis of retrospective data from a 19 month period when procalcitonin was implemented. Next, a retrospective quasi-experimental study was done using a control group of emergency department patients with a sepsis diagnosis. Data included 19 months prior to the implementation of procalcitonin.**Results:** In objective 1, the sample consisted of 165 sepsis cases and there was a positive correlation between lactic acid and procalcitonin values ($r=0.377$, $p < 0.001$). From the 165 sepsis cases who had positive blood cultures, procalcitonin had a sensitivity of 89.7%. In comparison, lactic acid was not as good a predictor as procalcitonin, its sensitivity at the current cutoff of 2.0 mmol/L was 64.9%. In objective 2, there post-procalcitonin samples were 165 cases and the pre-procalcitonin sample was composed of 69 cases. There was a significant decrease after the implementation of procalcitonin in cost of hospitalization compared to costs pre-implementation (Wilcoxon $Z = 2.034$, $p = 0.042$). Although this cost is highly correlated with length of stay, neither the hospital (Wilcoxon $Z = 0.006$, $p = 0.995$) or ICU length of stay (Wilcoxon $Z = 0.037$, $p = 0.970$), showed a difference with pre and post implementation.**Conclusion:** Our findings indicate that procalcitonin values had a higher predictive usefulness than the lactic acid. A consideration for lactic acid was to lower the cutoff to 1.4 mmol/L so its sensitivity is similar to that of procalcitonin but the specificity (45.7%) and positive predictive value (35.5%) were lowered. Based on information from objective 2, the decrease in costs could be associated with a variable outside of the length of stay, or the parametric test was not powerful enough to a show a decrease in length of stay, or the decrease in costs is a spurious association. Although procalcitonin is a relatively new test, it demonstrates to be a better marker for early diagnosis of sepsis and positively impact the health care practices in a community hospital setting as indicated in objective 1. Although this test is not routinely utilized to its full potential, it offers an opportunity to reevaluate the sepsis protocols as an alternative use of procalcitionin versus lactic acid for early diagnosis.

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Is There a Relationship Between Serum Fetuin A Levels and Hematological Parameters with Behcet Disease Activity

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Background: Behcet's disease (BD) is a multisystemic inflammatory condition which has unclear etiology. Serum fetuin A concentrations were shown to be inversely related with serum C reactive protein (CRP) concentrations and cytokines which are participating in inflammation, thereby fetuin A categorized as a negative acute phase protein (APP). Also Neutrophil / lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) values are suggested as simple and inexpensive inflammation markers. Fetuin-A, a glycoprotein is composed by two cystatin like domains and a smaller unrelated domain; also known as the alpha-2- Heremans-Schmid (HS)-glycoprotein, is produced principally by the liver and has an important role in normal and pathological situations, including insulin resistance, obesity, vascular and valvular calcification, bone metabolism regulation, tumor cell proliferative signaling and protease activity control.

Objective: We aimed to evaluate the association between serum concentrations of fetuin A, NLR, PLR and disease activity and clinical characteristics of BD.

Methods: The study population includes 53 BD patients (39 active, 14 inactive) and 31 healthy controls. Fetuin A, CRP, erythrocyte sedimentation rate (ESR), neutrophil, lymphocyte and platelet test were analysed and NLR and PLR values were calculated in all subjects.

Results: BD patients in active phase had significantly lower serum Fetuin A concentrations than both of passive BD($p=0.009$) and control ($p=0.006$) group . Mean serum levels of Fetuin A were 294.21±85.69 µg/mL in active BD patients and 374.84±118.02 µg/mL in passive BD patients and 359.64±63.46 µg/mL in control subjects.There was no significant difference between passive BD and control group fetuin A levels($p=1.000$). P/L ratio was significantly lower in active ($p<0.001$) and passive ($p<0.001$) BD patients than control group

Conclusion: Our findings suggest that serum Fetuin A levels are lower in patients with active BD. Fetuin A might be used in following the disease activity.

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Serum fetuin A levels and Hematological Parameters in Chronic Kidney Disease and Hemodialysis Patients for Assessing Inflammation

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Background: Chronic kidney disease (CKD), includes conditions that destroy the kidney and causes loss of its functions. Fetuin-A, also known as α-2 herman schemid glycoprotein belongs to the cystatin super family, a cluster of cysteine protease

inhibitors. It is mainly synthesized by liver and secreted into the bloodstream. Its production is closely regulated by the inflammatory status of the body. The objective of the current study is to examine the association between serum Fetuin A concentrations and some other basic inflammation markers (neutrophyl to lympcyte ratio(NLR), mean plathelet volüme(MPV) and C reactive protein(CRP)) in chronic kidney disease and hemodialysis patients.

Methods: This study subjects is composed of healthy volunteers (n=47) and two patient groups; chronic kidney disease patients (n=26) and hemodialysis patients (n=33). We measured serum glucose, urea, creatinin, total protein, albumin, sodium, potassium, calcium, phosphorus, iron, alkaline phosphatase (ALP), parathyroid hormone (PTH), ferritin and CRP levels by otoanalyzer and fetuin A levels by ELISA method. Also Complete blood count parameters analysed and NLR was calculated.

Results: There were significant difference in serum Fetuin A concentrations, NLR and MPV values among three groups ($p<0.001$,$p<0.001$,$p<0.001$). The correlation analyses revealed that fetuin-A negatively correlated with urea, creatinine, PTH, ferritin, and CRP concentrations (r: -0.349, -0.367, -0.295, -0.399, -0.550, respectively, $p<0.05$)

Conclusion: Fetuin A is lower than control group in CKD and hemodialysis patients, remarking as a negative acute phase reactant. NLR and MPV values are higher in CKD group comparing with control subjects. Determination of serum fetuin-A, NLR and MPV might present useful information to assess inflammation in chronic kidney disease and hemodialysis patients.

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External validation of lab data-based mortality risk scores in patients undergoing coronary catheterization

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Background: Risk scores based on results from simple laboratory tests such as the basic metabolic panel are being used more often in the acute care setting as they provide fast, reliable and accurate predictions of serious outcomes such as death and readmission. However few studies have evaluated the performance of these risk scores in different geographic locations. Our objective was to test the prognostic power of a laboratory data-based mortality risk score developed in Calgary, Alberta, Canada (population 1.4 million) in Edmonton - the second largest city in Alberta (population 1.3 million). **Methods:** Age, sex, CO_2, chloride, hemoglobin, MCHC, MCV, platelet count, potassium, RBC, RDW, sodium, eGFR, WBC, INR, provincial healthcare number and test verification date were extracted from the laboratory information systems of Calgary Laboratory Services and Alberta Health Services (November 2009-December 2015) and merged to patient demographic (age, sex, smoking status) and outcome data from the Alberta Provincial Project for Outcome Assessment (APPROACH) , a province-wide cardiac catheterization registry. We merged only the last lab panel up to 30 days prior to catheterization. Lab variables were divided into quintiles and programmed as four dummy variables to allow non-linear relationships. Using Calgary as a 'development' sample, logistic regression with a group LASSO penalty was used to select a panel of tests that yielded the highest c-index (measure of discrimination between deaths and survivors) and best calibration (difference from predicted vs actual death probabilities) slope p-value (non-significant = better calibration of model) for <60-day post-catheterization mortality and >= 60 day post catheterization mortality. Validation in Edmonton was done by multiplying scoring coefficients developed in Calgary by Edmonton patient values, and re-calculating c-indices, calibration slopes and slope p values. Model re-calibration was done by multiplying a scaling factor by Calgary coefficients if c-indices and calibration slopes did not match. Risk scores for each population were created by multiplying patient lab values by regression coefficients and adding the products together, after which discrimination and calibration were recalculated. **Results:** In the Calgary development sample, there were 14135 patients among which there were 216 deaths < 60 days, and 941 deaths >=60 days available for analysis. Final models contained age, sex, CO_2, Sodium, Chloride, hemoglobin, RBC, WBC, RDW, eGFR, and INR. The c-indices, calibration slopes and slope p-values for each score were: < 60 days: c=0.85, slope=1.01, slope p=0.75; >= 60 days: c=0.80, slope=0.99, slope p=0.73 - indicating good discrimination and model calibration for deaths < or >= 60 days after catheterization. In the Edmonton validation sample, there were 12394 patients among which there were 347 deaths < 60 days and 1073 deaths >= 60 days available for analysis. The c-indices, calibration slopes and calibration slope p-value for scores based on re-calibrated coefficients were: < 60 days: c=0.82, slope=1.05, slope p=0.07; >= 60 days: c=0.80, slope=1.02, slope p=0.05 - indicating similar discrimination but slightly worse calibration. **Conclusion:** Lab-based risk scores developed to predict mortality performed similarly in two large urban centres in Alberta, Canada. Our long-term plan is to implement these scores in coronary catheterization labs across Alberta.

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Frequency of Mutations in the Galactose-1-Phosphate Uridyl Transferase Gene in California: Findings from an eight year study

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Background: The deficiency of galactose-1-phosphate uridyl transferase (GALT) which converts galactose-1-phosphate to uridine diphosphate galactose results in an inherited metabolic disorder: classic galactosemia. Common mutations/variants of this enzyme are well-identified: IVS2-2A>G, S135L, T138M, Q188R, L195P, Y209C, L218L, K285N, and N314D. The California newborn screening program uses newborns' dried blood spots to screen for GALT deficiency. Follow-up testing for presumptive positive cases uses a whole-blood specimen to identify common mutations in the GALT gene. Prior studies have reported a high frequency of some mutations, such as Q188R, in select populations. Other mutations have been described as more common in certain race/ethnic groups, including the IVS2-2 mutation, which has been reported as being more prevalent in Hispanic populations. Using data from eight years of newborn screening in California, our aim was to describe the frequency of the most common GALT mutations in the racially and ethnically diverse California Population.

Design: The Newborn Screening Program, administered by the California Department of Public Health, screens for GALT deficient newborns as part of routine newborn screening. Each year, approximately half a million newborns are tested for GALT deficiency using the API 300 Analyzer using dried blood spot specimens. Presumptive positive cases are followed up by DNA testing using a well-defined single nucleotide extension method to identify common GALT gene mutations. We studied the frequencies of 7 mutations and 2 variants in newborns tested between July 2008 and June 2016.

Results: Out of nearly 4 million babies screened in California during the 8-year period, 247 GALT-deficient newborns had follow-up mutation analysis. The Q188R (66.40%) mutation and the variant N314D (66.40%) had the highest frequency in one or 2 alleles. This was followed by IVS2-2G (7.69%), S135L (6.88%), K285N (2.43%), L195P (2.02%), Y209C (0.81%), and L218L (0.4%). The T138M mutation was not detected in any newborns. The frequency of homozygosity was 6.07% for the Q188R mutation, 4.45% for the N314D variant, and 1.21% for the S135L. We also found a higher prevalence of the IVS2-2 mutation, known to be more common in Hispanic populations.

Conclusion: To the best of our knowledge this is the largest study to describe the frequency of GALT mutations in a racially and ethnicity diverse population. This is also the first study to use single nucleotide extension to study the IVS2-2 mutation. In concordance with other studies, the Q188R was the mutation with a very high prevalence; and similar to other studies with extremely low frequency for T138M mutation, none of the specimens were detected with this mutation. The low percentage of L218L is due to the GALT deficient population being tested. L218L variant increases GALT and we didn't expect high frequency of this variant in our GALT deficient population. Some of our findings were similar to studies from Texas, another state with a high Hispanic population. This includes a higher prevalence of the N314D and IVS2-2 mutations. The frequency of the IVS2-2 mutation was even higher than the Texas study and may reflect more births to newborns with Hispanic origin in California.

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Prevalence and laboratory characterization of monoclonal gammopathy of undetermined significance by physical examination in Beijing

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Background

Monoclonal gammopathy of undetermined significance (MGUS) is a benign condition present to monoclonal plasma cell proliferation in the people aged more than 50 years old. No studies have far evaluated a large population of apparently healthy adults in ethnically Chinese population. To gain further understanding about the prevalence and laboratory characters of MGUS in China mainland, the current study was designed as a general analysis that know the related lab features in people who underwent physical examinations in Beijing with MGUS.

Methods

A total of 44443 adult patients from the physical examination center were retrospectively enrolled in the study. The age range of these subjects was from 18 to 96 years old and the mean age was 42.44±12.62 years. Capillary serum protein electrophoresis (SPE) was carried out as main screening test on the subjects. Serum samples which were found monoclonal bands or suspicious monoclonal protein (M protein) were subjected to agarose gel immunofixation electrophoresis (IFE) to identify. Serum free light chain (sFLC) and β2 micro globulin were quantified to the samples which IFE results were positive.

Results

A total of 295 patients were diagnosed as MGUS according to the definition and suggestion of clinicians. The overall prevalence of MGUS was 0.66%. The prevalence was significantly higher in males than that in females (0.78% vs. 0.52% respectively, P=0.001, P<0.01). MGUS prevalence also significantly increased with age and it was 1.05%, 1.79%, 4.17%, 4.53% respectively in subjects older than 50, 60, and 70 and 80 years old. Immunofixation electrophoresis analysis (IFE) showed that IgG kappa (39.32%), IgG lamda (32.88%) and IgA lamda (12.54%) were the predominant monoclonal immunoglobulin pattern in these MGUS subjects. Double-type and lamda light chain pattern were simultaneously found in MGUS patients. The monoclonal immunoglobulin concentration was from 0.02 g/dL to 1.92 g/dL in the MGUS patients. The median concentration was 2.80 g/dL and 95% confidence interval was 3.49 g/dL to 4.50 g/dL. The serum free light chain (sFLC) κ: λ ratio range was from 0.00075mg/L to 34.077mg/L. There were respectively 32 (11.03%) and 33 (11.38%) serum samples which showed sFLC κ: λ ratio lower or higher than the reference range. We found 12 (4.17%) samples in MGUS were higher than 3.5 mg/L and 4 (1.39%) samples were higher than 5.5 mg/L with the concentration of serum β_2-microglobulin.

Conclusions

The overall prevalence of MGUS in China mainland was 0.66%. The prevalence was gender and age dependent. Some main lab characters of MGUS patients were evaluated in Chinese population.

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Diagnostic value of different detecting technologies in antinuclear antibody (ANA) in autoimmune diseases

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Background: Autoimmune diseases refer to immune reaction between the body antibody and its own antigen, which results in tissue damage. Antinuclear antibodies (ANA) play an important role in the diagnosis, treatment monitoring and prognosis judgement of autoimmune disease. Antinuclear antibodies (ANA) is an important screening index of autoimmune disease . But detection methods of ANA are varied.So our study is to investigate the positive rate and the coincidence rate between different methods,and our further research is to investigate the inconsistent phenomenon and the solutions, in order to provide more valuable reference information for clinical diagnosis, treatment monitoring and prognosis judgement in autoimmune diseases. **Methods:** We collected 61 cases of patients with systemic lupus erythematosus (SLE), 181 cases of patients with autoimmune diseases but without SLE, 476 cases of patients without immune diseases, 710 cases of volunteers for control group. ANA was detected by ELISA and indirect immunofluorescence (IIF) method. 12 kinds of specific autoantibodies in ANA were detected by western blot method (LIA).

Results: Average coincidence rate between ELISA and IIF method to detect the ANA was 77.7% in the four groups of participants. The results of ANA detected by ELISA method were positively correlated with that by IIF method (correlation coefficient of 0.598, P < 0.01). Then we study the inconsistent results of ANA respectively detected by IIF method and LIA method,we found that patients with AID and no AID groups both existed the phenomenon of IIF ANA (+) LIA ANA (-), their fluorescence titers were given priority to with 1:100.Their fluorescence modes were given priority to with granularity (S) in AID group, significantly higher than that of no AID group; no AID group fluorescence mode was given priority to with type cytoplasm particles (Cyto). At the same time, the study found that patients with IIFANA (-) LIA ANA (+) were mostly AID patients (73.3%), the ratio was higher than no AID group, among these patients ,AID patients were with SSA/Ro60, SSA/Ro52, SSB/La as the main positive autoantibodies, rather than no AID patients with anti - Sm, SSA/Ro52, SSB/La, Cenp B as the main positive antibodies. SLE group, the other AID group compared with control group, in addition to Jo - 1 (LIA), the positive rate of other specific autoantibodies were Statistic different (P < 0.05). Among these specific autoantibodies,we collect six indexes well related with SLE: ANA, anti dsDNA antibodies, nRNP/Sm, Sm, AnuA, AHA to multi-index joint detection . In SLE group, the positive rate of ANA ,dsDNA, AnuA joint detection model was higher than other detection models(ANA, dsDNA, Sm model;ANA, dsDNA, AHA model,;dsDNA, Sm model).

Conclusion: Different detecting technologies in ANA have differences between sensitivity and specificity.If you use only one kind of methods ,it is likely to cause the positive ANA result omission and AID missed diagnosis. Therefore, clinical application, especially in patients with clinically suspected AID, we should carry out ELISA-ANA or IIF - ANA screening and LIA-ANA for various specific autoantibodies detection at the same time, and pay attention to multi-index joint detection when we diagnose autoimmune diseases.

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An Evaluation of the Automated Analysis of Common Urinary Sediments on the Sysmex UX-2000

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Background: Urinalysis is a routinely ordered test to screen for urinary tract infections and renal abnormalities. During a recent open tender process, we evaluated the UX-2000, an automated test strip and particle analysis urinalysis instrument, to supersede our existing UF-1000i analyser. A comparison of the common urine sediments between the two instruments was used to evaluate the UX-2000.

Methods: Fresh mid-stream urine was collected from 113 patients in a multi-disciplinary acute care hospital and promptly sent to the laboratory for examination. These samples were analysed on both analysers concurrently, using an established workflow. The principle of analysis for both instruments is based on fluorescence flow cytometry. The parameters for the evaluation included: Red blood cells(RBCs), White blood cells(WBCs), Epithelial cells(ECs) and Bacteria. Trueness, imprecision, clinical sensitivity and clinical specificity were determined.

Results: Trueness studies against the UF-1000i yielded a relationship of y=0.85x+4.36, y=1.01x+0.95, y=0.97x+0.43, y=1.17x-20.14 for RBCs, WBCs, ECs and Bacteria respectively. The correlation coefficients ranged between 0.978 and to 0.999.

Analytical specificities were 98.1%, 95.6%, 94.6% and 97.9% while analytical sensitivities were 97.9%, 96.4%, 88.9% and 90.6% at their cutoffs of >13 cells/ul, >10 cells/ul, >7 cells/ul and >20 cells/ul for RBCs, WBCs, ECs and bacteria, respectively.

The imprecision study performed using low level quality control material yielded a Coefficient of Variation of 5.4%, 7.9%, 9.8% and 9.4% for RBCs, WBCs, ECs and Bacteria respectively. Additionally, the imprecision study using high level quality control material yielded a Coefficient of Variation of 2.6%, 1.3%, 4.0% and 4.8% for RBCs, WBCs, ECs and Bacteria respectively. These values fall within the manufacturer's recommendations of 10% for RBCs and WBCs, 30% for ECs and 20% for Bacteria.

Conclusion: Our study showed that the UX-2000 had an acceptable performance and is a suitable replacement for our current analyser, the UF-1000i. We found good correlation between the two analysers for the automated quantification of RBCs, WBCs, ECs and Bacteria. In addition, the UX-2000 analyser's built-in automated Dipstick analyser allows for lesser hands-on time which, which translates to increased productivity.

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Development and evaluation of a serum biomarker panel in diagnosis of lung cancer

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Background

Lung cancer is the most common cancer and leading cause of cancer-related deaths worldwide. With the progress of tumor stage, the prognosis was significantly worse. Thus, early diagnosis of lung cancer is important to improve patient survivals. Blood-based biomarkers are easily accessible measurements that define high-risk patients and enhance diagnostic capabilities. Although published data on individual

serum biomarkers for lung cancer have shown limited sensitivity and specificity, the combination of several biomarkers could improve the detection of early-stage lung cancer. Thus, the present study is to investigate the clinical diagnosis model for lung cancer diagnosis.

Methods

A total of 230 lung cancer patients (cancer group) and 80 subjects with benign lung tumors (control group), were recruited from Da'lian Medical University 2nd Hospital in China. The study received ethical approval from the site.

Serum CEA, SCC, CYFRA21-1, HE4 and ProGRP levels were examined by the ARCHITECT i2000(Abbott,USA).

Results

We examined the diagnostic value of CEA, SCC, CYFR211, ProGRP and HE4 individually or in combination for lung cancer using ROC curve analysis. The optimal cut-off value of each biomarker was obtained to yield the maximum Youden index.

Compared with control, AUC of individual biomarker CEA, SCC, CY211, ProGRP and HE4 exhibited from 0.648 to 0.857. To increase the diagnostic value, these five biomarkers were combined and equation model was set up. The equation was P = 0.121*CEA + 0.568*SCC + 0.513*CY211 + 0.011*ProGRP + 0.036*HE - 3.972, with cut-off of 0.729. AUC in biomarker combination increased to 0.907 with sesitivity of 70.6% and specificity of 94.90%. According to sub-type analysis, biomarker panel combination showed better performance in SCC(Squamous carcinoma) and SCLC(Small cell lung cancer) compared with AD(Adenocarcinoma).

Conclusions

This study established a biomarker combination model for lung cancer diagnosis with significant clinical performance.

Table 1 Evaluation of a serum biomarker panel for lung cancer

	AUC	95%CI	sensitivity	specificity	Youden's index
LC VS Control					
CEA	0.717	0.672-0.763	36.20%	94.90%	0.311
SCC	0.702	0.655-0.748	32.40%	95.50%	0.279
CY211	0.758	0.715-0.8	44.70%	94.90%	0.396
pro-GRP	0.648	0.599-0.697	29.00%	94.90%	0.239
HE4	0.857	0.825-0.889	56.70%	94.90%	0.516
panel	0.907	0.881-0.932	70.6%	94.90%	0.655
AD vs Control					
CEA	0.74	0.69-0.79	43.20%	94.90%	0.381
SCC	0.674	0.619-0.728	28.10%	95.50%	0.236
CY211	0.696	0.643-0.750	36.50%	94.90%	0.314
proGRP	0.593	0.536-0.651	18.20%	94.90%	0.131
HE4	0.829	0.789-0.870	50.50%	94.90%	0.454
panel	0.875	0.840-0.909	60.40%	94.90%	0.553
SCC vs Control					
CEA	0.685	0.61-0.76	18.70%	94.90%	0.146
SCC	0.906	0.859-0.954	60.70%	95.50%	0.562
CY211	0.91	0.858-0.961	75.40%	94.90%	0.703
proGRP	0.634	0.547-0.721	27.90%	94.90%	0.228
HE4	0.93	0.895-0.965	70.50%	94.90%	0.654
panel	0.987	0.975-0.999	93.4%	94.90%	0.883
SCLC vs Control					
CEA	0.658	0.558-0.759	28.9%	94.90%	0.238
SCC	0.524	0.419-0.63	11.1%	95.50%	0.066
CY211	0.82	0.747-0.894	42.20%	94.90%	0.371
proGRP	0.928	0.87-0.986	91.10%	94.90%	0.86
HE4	0.88	0.812-0.948	73.30%	94.90%	0.682
panel	0.989	0.000-1.0000	95.00%	94.90%	0.899

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Clinical evaluation of PIVKA-II in Hepatocellular carcinoma diagnosis in Chinese population-a single center analysis

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Background and Aims

Liver cancer is a leading cause of cancer-related deaths in Asia. There are serval subtypes of liver cancer, of which hepatocellular carcinoma (HCC) is the major one. Persistent viral infections with hepatitis B virus (HBV) and/or hepatitis C virus (HCV) contribute to the pathogenesis of HCC. Unfortunately, there are around 250,000,000 HBV carriers in Asia, presenting the unmet medical needs for liver health management and early HCC diagnosis.

Protein induced by vitamin K absence or antagonist-II (PIVKA-II) is an abnormal des-gamma-carboxyprothrombin (DCP) in patients with vitamin K deficiency and recently showed the clinical value in HCC diagnosis. Most of the clinical data is from Japan. However, its clinical application still needs more evidence supports in Asian population. In addition, most of HCC patients in Japan are HCV related while other Asian countries are HBV related. Thus, we initiated an Asian study on the application of PIVKA-II in HCC diagnosis and differential diagnosis including China, Singapore, Vietnam and Thailand. Here we report the preliminary results from a site in Eastern China.

Methods

A total of 161 cases of HCC and 136 cases of cirrhosis were recruited from Eastern Hepatobiliary Surgery Hospital in China. All the patients' information were recorded and validated. The study received ethical approval from the site.

PIVKA-II levels were examined by the ARCHITECT PIVKA-II assay(Abbott,USA), which is a two-step sandwich immunoassay, using chemiluminescent paramagnetic microparticle technology for quantitative determination of PIVKA-II.

Results

Distributions of serum PVKA-II levels were significantly higher in HCC patients compared with cirrhosis patients. P value was <0.001 comparing HCC with cirrhosis group. In addition, we depicted ROC curve to evaluate the diagnostic performance of PIVKA-II as a biomarker . As a result, our curve showed the area under the ROC curve (AUROC) for PIVKA-II to be 0.87(95% confidence interval, CI: 0.82 - 0.91) in all HCC patients. Under different cut-off values , the sensitivity and specificity varied. When the sensitivity reached 100.0%, the specificity was only 5.1% at the cut-off of 11.9 mAU/ml. When it was set at 40.0 mAU/ml(the most common used cut-off value), the sensitivity was 84.2% with specificity of 95.5%. If the specificity was set-off at 100.0%, the sensitivity was 52.0% and the cut-off value was 256.4 mAU/ml.

Conclusions

The preliminary data supports the clinical application of PIVKA-II in HCC diagnosis in China population. However, the detailed clinical diagnosis strategy is still under investigated.

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A Prospective, Observational Study of the Clinical Decision Impact of the Prostate Health Index (*phi*) Test in a Urology Practice Setting

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Objective

Data are limited on the clinical utility and cost effectiveness of new tests to detect PCa, and additional evidence is needed to determine their impact on physician decision making and patient care. The objective was to determine the impact of *phi*

on patient management, by comparing physician responses to a questionnaire pre- and post-*phi* testing. The impact on decision to biopsy and proportion of negative biopsy results obtained was also evaluated.

Methods

An IRB approved observational study was conducted at four large urology group practices using a two-part questionnaire completed by the urologist. Patient recommendations were recorded before and after the *phi* score. A historical control group was queried from electronic medical records for eligible patients who did not receive a *phi* test. 502 men were prospectively, consecutively enrolled, and 575 additional men were included in the control arm, after exclusions. Subjects had PSA concentrations between 4-10 ng/mL, were ≥50 years of age, had a non-suspicious DRE, no prior suspicious or positive prostate biopsy, and were referred for biopsy based on elevated PSA. The PSA, free PSA, and [-2]proPSA concentrations were determined using the Beckman Coulter Access 2 Immunoassay Analyzer. *phi* was calculated as ([-2]proPSA/free PSA) x $PSA^{½}$.

Results

The phi score impacted physician decisions in about 74% of cases (Figure 1), including performing biopsies when the *phi* score was elevated and identifying biopsies that may have been unnecessary or that could be delayed. In instances where the biopsy decision was unchanged, questionnaire responses showed *phi* helped confirm decisions and made discussions with patients easier.

Figure 1.

	***phi* score group**					
Did *phi* score impact decision to Biopsy or Monitor patient?	**0-26.9 N (%)**	**27.0-35.9 N (%)**	**36.0-54.9 N (%)**	**55+ N (%)**	**Total**	**Percent of Total**
Yes, *phi* score impacted physician's decision	81 (22.1)	85 (23.2)	130 (35.6)	70 (19.1)	366	**73.5**
No, *phi* score did not impact physician's decision	35 (26.5)	34 (25.8)	44 (33.3)	19 (14.4)	132	**26.5**
Total	116 (23.3)	119 (23.9)	174 (34.9)	89 (17.9)	498 *four missing	

Pre-*phi* Decision Biopsy				Pre-*phi* Decision Monitor					
Post-*phi* Decision Biopsy N = 169		Post-*phi* Decision Monitor N = 145		Post-*phi* Decision Biopsy N = 70		Frequency and type of testing *unchanged* N = 18		Frequency and type of testing *changed* N = 96	
Yes *N = 84 (50 %)*	No N = 85	*Yes* *N =145 (100%)*	No N = 0	*Yes* *N = 70 (100%)*	No N = 0	*Yes* *N = 17 (94 %)*	No N = 1	*Yes* *N = 50 (52 %)*	No N = 46

Conclusions

Results demonstrate that *phi* positively impacts patient care. The biopsy rate was significantly lower, and the percentage of GS ≥ 7 was significantly higher, post-*phi* testing versus controls, demonstrating a reduction in unnecessary biopsies and a selective shift toward identifying clinically significant PCa.

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Serum Oxidative and Antioxidative Parameters in Obstructive Sleep Apne Syndrome Patients

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Background: The purpose of this study was to evaluate markers of systemic oxidative stress and antioxidant capacity in subjects with severity of OSAS.

Methods: A total of 106 OSA patients were included in the study (18 controls, 14 with mild, 14 with moderate, and 60 with severe OSA). Patients were grouped according to apneahypopnea index (AHI) as mild, moderate and severe OSA. Patients with AHI<5 served as control group. Known risk factors for oxidative stress, such as age, sex, obesity, smoking, hypelipidemia, and hypertension, were investigated as possible confounding factors. Plasma arylesterase, total oxidative stress (TOS), total antioxidant capacity (TAC), total thiol, catalase (CAT) levels were measured for all patients.

Results: The mean age was 52.49 ±12.9 years and 40.6 % (43/106) of the study population was female. Plasma arylesterase, TOS, TAC, total thiol, and CAT plasma values were not different between mild, moderate, severe OSA groups and controls ($p > 0.05$). Catalase levels were significantly lower in women patients with severe OSA compared to healthy women controls ($p < 0.05$). There was a negative correlation between AHI and serum total thiol levels ($r= -0.289$, $p<0.05$) in severe OSA groups.

Conclusion: The present prospective study provides evidence that OSA might be associated with decreased antioxidant burden possibly via catalase way.

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Where we Stand on Omission of Biopsy for a Diagnosis of Celiac Disease

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Background:

Duodenal biopsy has remained the gold standard for a Celiac disease (CD) diagnosis for decades. However, improved diagnostic accuracy of serological testing and potential risks associated with endoscopy in children has allowed omission of biopsy to become the standard of care in Europe under the 2012 ESPGHAN Guidelines. The diagnostic algorithm allows symptomatic children with screening tissue transglutaminase IgA (tTG-IgA) titer more than 10x upper limit of normal to undergo EMA and HLA testing. To date, this is the first widely accepted alternative to biopsy. Our aim is to retrospectively examine the performance of tTG-IgA at our institution to assess the feasibility of shifting towards a non-invasive diagnosis for CD in a specific pediatric population in the United States.

Methods:

Consecutive tTG-IgA serology was obtained on children aged 2 to 18 years from November 2015 to October 2016. Serology was performed using an immunoassay on QUANTA-Lite® tTG-IgA from INOVA Diagnostics and positive results reported when ≥4 U/ml. Patients with IgA deficiency and lab results/biopsy from outside institutions were excluded. Biopsy findings were graded according to Marsh-Oberhuber classification.

Results:

Total tTG-IgA serology performed yielded 2723 results. The distribution and characteristics of patients are summarized in Table 1. The sensitivity, specificity and PPV of tTG-IgA is 86.7%, 99.4% and 84.7%, respectively. According to 2012 ESPGHAN guidelines, duodenal biopsy may have been omitted in 38% of patients depending on EMA and HLA status.

Conclusion:

We report high sensitivity and specificity of tTG-IgA at our institution, and is comparable to the literature. These results strengthen the notion that this simple screening test, when paired with appropriate symptomatology, can reliably identify a select population in whom EMA and HLA may be warranted, and biopsy omitted. In order to initiate a non-invasive transition, more emphasis is necessary on helping clinicians better understand the performance of celiac serology testing.

Table 1.

	Duodenal Biopsy	
tTG-IgA	**Positive**	**Negative**
Positive	**78** 52 - Titer >10x ULN (67%) 35 - GI symptoms 32 - Marsh 3 lesion	**14** 5 – Titer >10x ULN (36%)
Negative	**12** 3 with Marsh 2 (25%): 1 - EMA+ 1 - HLA-DQ2+ 1 - Dermatitis Herpetiformis 9 with Marsh 1 (75%): 3 - Intestinal infection 2 - Peptic injury 2 - Crohn's disease 1 - Hyperthyroidism 1 - Dysmotility	**2619**

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Comparison of Active B12 with Total B12 and Methylmalonic Acid in patients with cognitive impairment

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Background: Patients with vitamin B12 deficiency are at risk for developing neurological abnormalities and methylmalonic academia. Although serum methylmalonic acid (MMA) can be used to confirm B12 deficiency, this test is not readily available in most laboratories. Instead, total B12 measurements are used as a surrogate, although it does not correlate well with MMA. Active B12 assays, which only measure B12 bound to transcobalamin, have been suggested to be a better marker of B12 deficiency than total B12. In this study, we evaluated the performance of active B12 compared to total B12, MMA and neurological evaluation.

Methods: This study was approved by our institutional ethics committee and patients were recruited at neurology clinics. Once consent was obtained, patients received neurological evaluation as per standard of care. Patients also had blood drawn for total B12, active B12 and MMA testing. Total B12 was measured using a Roche Cobas e601 platform. Active B12 was measured using Abbott Active B12 reagent on an Abbott Architect. MMA was measured by LC-MS/MS.**Results:** To date, 62 patients have been recruited into the study. These patients are a mixture of those with normal cognition, cognitive impairment and dementia. Preliminary results showed total B12 correlated well with active B12 (y=0.4254x-49.941; R2=0.6642). However, total B12 and MMA as well as Active B12 and MMA showed poor correlation. This relationship was maintained when only samples with MMA greater than 250 pmol/L were included. Data from neurological assessments of each patient is being collated and will be presented at the meeting.

Conclusion: Our preliminary results showed that B12 deficiency can be assessed by either active B12 or total B12. However, active B12 may not be a suitable surrogate for MMA analysis. Clinical information will be correlated with biochemical analysis and the results will be present completely in July.

A-145

Genetic Risk Prediction for Developing Age-related Macular Degeneration and Disease Progression

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Purpose: Age-related macular degeneration (AMD) remains the leading cause of irreversible visual loss among the elderly in developed countries. The earlier asymptomatic form of AMD is characterized by the formation of confluent drusen in the macula, while advanced AMD includes geographic atrophy (GA) and choroidal neovascularization (CNV). It is likely that the management of patients with AMD will be influenced by assessment of genetic risk. The aim of this study was to develop a separate class prediction algorithm for AMD lifetime risk assessment and disease progression from intermediate AMD to either GA or CNV based on individual genetic profiles.

Methods: DNA samples were genotyped using the AutoGenomics INFINITI platform. AMD panel (for research use only) included ABCA1(rs1883025); APOE(rs429358, rs7412); ARMS2(rs10490924); C3(rs2230199); CCDC109B(rs17440077); CETP(rs3764261); CFB(rs4151669, rs522162); CFH(rs1048663, rs1061170, rs10737680, rs1329428, rs2274700, rs3766405, rs412852); CFI(rs10033900); COL8A1(rs13095226); HTRA1(rs11200638); LIPC(rs493258, rs10468017); LPL(rs12678919); TIMP3(rs9621532) and VEGFA(rs3025000, rs943080). Class prediction model building and testing were performed using TreeNet software (Salford Systems, San Diego, CA). The binary logistic regression analysis with a 10-fold cross-validation method was applied in the algorithm development.

Results: We genotyped the selected 25 SNPs in 893 cases with advanced AMD (consisted of 206 GA and 687 CNV), 265 cases with intermediate AMD and 384 controls. Progression was defined as transition from intermediate to advanced AMD, either GA or CNV, in the worse eye during a follow up visit. We selected only patients with intermediate AMD who did not progress within 7 years to advanced stages and considered them as non-progressors. For model building we applied a 'shaving' technique, in which the predictors are ranked from top to bottom (the most important to the least important) at every step when the bottom predictor is removed and the model is rebuilt. This technique allowed us to choose three distinct models with the best performance and further evaluate. As a result, we developed three class prediction algorithms: 1) for AMD lifetime risk assessment in AMD patients versus controls based on 13 SNPs; 2) for progression to GA in GA progressors versus non-progressors based on 9 SNPs; 3) for progression to CNV in CNV progressors versus non-progressors based on 10 SNPs. The ROC of the model for AMD risk for the test set was 0.75 with 70% sensitivity and 68% specificity. The ROC of the model for progression to GA for the test set was 0.63 with 53% sensitivity and 72% specificity. The ROC of the model for progression to CNV for the test set was 0.55 with 55% sensitivity and 52% specificity.

Conclusions: Our results suggest that the INFINITI AMD panel can be successfully used for the AMD lifetime risk assessment as well as disease progression. In addition, risk of developing AMD and disease progression can be further improved when the panel is combined with environmental factors such as age, smoking and other variables. The proposed approach to AMD risk determination, separate for lifetime risk and disease progression, might provide a useful clinical tool and be potentially applied toward more personalized care.

A-146

HE4 as a diagnostic and follow-up biomarker in non- small cell lung cancer

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Abstract

Background

Early detection of non-small cell lung cancer (NSCLC) cases is crucial since nearly one third of them are unresectable during diagnosis and also the recurrence rates are high following treatment. Human epididymis protein 4 (HE4) is predominantly expressed in a variety of normal human tissues including epididymis, epithelial cells of proximal airways and the female genital tract. HE4 has emerged as one of the most promising diagnostic and prognostic biomarker in epithelial ovarian cancer. High levels of HE4 have also been detected in lung, breast and pancreas cancers. Thus, in this study we aimed to evaluate both the diagnostic performance and the post-resection progress of serum HE4 in patients with NSCLC.

Methods

Thirty-one patients who had benign lung disease (group 1) were compared with the same number of patients with resectable NSCLC (group 2). Blood samples were collected in serum separator tubes and were centrifuged at 1500g for 10 minutes (Rotanta 460). HE4 levels were measured by chemiluminescent microparticle immunoassay at ARCHITECT *i*2000SR immunoassay analyzer (Abbott Diagnostics) at the time of diagnosis and following surgery - at post-operative 1st month. The cut-off limit for serum HE4 was considered 70 pmol/L.

Results

The serum HE4 in NSCLC group [median: 89.70 (58.10-397.00)] pmol/L was significantly higher than the benign group [median: 42.60 (28.10-198.90)] pmol/L, respectively ($p< 0.001$). HE4 levels in NSCLC group significantly decreased from 89.70 (58.10-397.00) pmol/L to 71.50 (41.70-232.30) pmol/L following pulmonary resection

($p<0.001$). In advanced stages (stage III and IV) the decrease in serum HE4 levels [25.30 (10.50-164.70)] pmol/L was significant than the decrease in early stages (stage I-II, [14.60 (14.20-133.60)] pmol/L ($p=0.025$). According to ROC analysis, the area under the curve (AUC) of HE4 was 0.921 (95% CI, 0.843-0.998), ($p< 0.001$). Both the sensitivity and specificity of HE4 as a biomarker was found 87.1%.

Conclusion

Our data demonstrated that HE4 is a potential biomarker for the diagnosis of NSCLC with high sensitivity and specificity. We believe that HE4 levels could also be used to monitor NSCLC recurrences and treatment response during follow-up.

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Serum Growth Arrest Specific Protein 6(Gas-6) Levels in Patients with Schizophrenia

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Background: We have investigated serum growth arrest-specific protein 6 (GAS-6) levels from patients with schizophrenia divided into acute phase remission phases as well as control group.

Methods: This study was conducted in Psychiatry Department of Istanbul University Cerrahpasa Medical Faculty. The patients who were diagnosed with schizophrenia after regular psychiatric examination according to DSM-IV criteria (n=22) as well as control subjects were included in the study. Schizophrenia patients with acute phase and remission phase were evaluated by Positive and Negative Syndrome Scale (PANSS) and Clinical global Impression Scale (CGI-S). The serum GAS-6 levels of schizophrenia patients during acute phase and remission phase were compared with the serum GAS-6 levels of healthy controls. Serum GAS-6 levels were measured by commercial ELISA development kit (R&D).

Results: No difference was found in serum GAS-6 levels among the three groups; schizophrenia with acute phase, schizophrenia with remission phase, and controls. There were no correlations between serum GAS-6 levels and PANSS and CGI scores.

Conclusion: To reach a definitive data and better interpretation about the relationship between GAS-6 and schizophrenia, future studies with larger groups of patients with schizophrenia subdivided by drug naïve and treated with antipsychotics/other treatment modalities and controls are needed.

A-149

Serum Gas 6 and Omentin Levels and relationship with Flow mediated dilatation , Aortic distensibility , Left ventricule mass index and disease severity in Patients with Psoriasis

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Background: *Growth arrest-specific gene 6 (*GAS6*) encodes a vitamin K-dependent protein secreted by* endothelial cells, vascularsmoothmuscle cells,and adipocytes *that regulates inflammation, insülin resistance, angiogenesis, and atherosclerotic plaque formation. The level of GAS6 expression is associated with plaque stability and stroke.* Changing in aortic distensibility (AoD) may reflect the features of the atherosclerotic process. Omentin, a novel adipokine secreted by the stromal vascular cells of adipose tissue, is considered associated with vascular, metabolic, and various chronic inflammatory diseases. Psoriasis is an autoimmune, inflammatory and chronic disease.This study aimed to determine the association between serum Gas6 and omentin levels with BMI, insulin resistance, flow mediated dilatation , Aortic distensibility and Left ventricule mass index in Patients with Psoriasis

Methods: The study was conducted on 30 healthy subjects (mean age: 41 ± 10 years) who were free of coronary risk factors and 52 patients with psoriasis(mean age: 41 ± 10 years).Body mass index were calculated. Circulating glucose, cholesterol , insülin, HbA1c, CRP, Gas6 and omentin levels analysed and insulin resistance were determined.Gas 6 and omentin were anaysed with ELISA method with commercially available kits(Biovendor ,Czech Republic) Transthoracic echocardiography was used to measure the Beta index , aortic distensibility (AoD), left ventricular mass index.Flow mediated dilation was measured with high resolution B mode ultrasound machine (Toshiba, aplio XU) with a 7.5 MHz linear transducer.

Results: Patients and control group were similar about age, body mass index, waist circumference and sex distribution.Insulin resistance (HOMA-IR) was high significantly in psoriasis patients.Levels of serum Gas6 levels were significantly higher ($p<0.001$) in patients group whereas omentin were significantly lower($p.0.001$). Aort distensibility and beta index were low in patients group($p:0.01$ and $p:0.02$ respectively). Also serum Gas 6 levels were positive and significantly correlated with HOMA-IR ($p:0.020$,$r:283$) and left ventricule mass index($p<0.01$,$r:689$). In addition, serum omentin levels were were positive and significantly correlated withwaist circumference($p:0.01$, $r:0.600$). Disease severity(PASI psoriasis area and severity index) was not correlated with any parameter in the study.

Conclusion: Circulating Gas6 and omentin levels and aort distensibility and beta index are significantly different in two groups. Serum Gas 6 levels are strongly correlated with insülin resistance status and left ventricule function status. Gas 6 may play a role assessing insülin resistance and left ventricule function status in patients with psoriasis.

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Risk assessment of opioid addiction with a multi-variant genetic panel involved in the dopamine pathway

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Background: More than 116 million people worldwide are struggling with chronic pain and most require prescription drugs. In the US, opioid prescription misuse and heroin use accounted for the majority of accidental overdose deaths in 2014. Genetic factors play a key role in opioid prescription addiction, but are generally not evaluated in clinical practice. Currently, there is no objective way for practitioners to identify pain patients in medical management who are at risk to abuse or become addicted to prescribed medication or to identify those pain patients who will require high dosages or an unusual regimen of medication. The purpose of this study is to assess a risk of developing prescription opioid addiction with a multi-variant addiction panel involved in the mesolimbic dopamine system.

Methods: We genotyped samples for 16 single nucleotide polymorphisms (SNPs) involved in the brain reward pathways from 70 patients diagnosed with prescription opioid/heroin addiction and 68 normal control patients with a multiplexed film-based microarray technology. The addiction panel targets 16 mutations: 5-HTR2A (rs7997012), 5-HTTLPR (rS25531), COMT (rs4680), DRD2 (rs1800497), DRD1 (rs4532), DRD4 (rs3758653), DAT1 (rS6347), DBH (rs1611115), MTHFR (rs1801133), OPRK1 (rs1051660), GABA (rs211014), OPRM1 (rs1799971), MUOR (rs9479757), GAL (rs948854), DOR (rs2236861) and ATP-BCT (rs1045642). The genotyping data were subjected to a class predication model building with 10-fold cross validation for testing. A risk score from 1 to 100 was further computed with a score over 52 representing an elevated risk of addiction.

Results: The receiver operating characteristic (ROC) for the model was 0.78 with 76% sensitivity (95% CI: 84 - 85) and 72% specificity (95% CI: 60 - 82). PPV is 74% and NPV is 74%. Fifty-Three of 70 (75.7%) addicts and 19 of 68 (27.9%) normal controls showed an addiction risk score over 52. ($X2=31.55$;$df=1$;$P<.05$).

Conclusion: The prediction algorithm with this multi-variant genetic panel can be used for prescription opioid addiction risk assessment. By identifying patients with high risk to prescription opioid addiction along with mutation status of cytochrome p450 genes involved in therapeutics, it may provide information to physicians to improve therapeutic decisions in pain management and prevent abuse and addiction.

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Performance Evaluation of the VITROS® NephroCheck® Test*

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Acute kidney injury (AKI) is a complex disorder with a high mortality due to comorbidities and management challenges, especially in the critically ill patient. The VITROS® NEPHROCHECK® Test quantitatively measures Tissue Inhibitor of Metalloproteinase 2 (TIMP-2) and Insulin-like Growth Factor Binding Protein 7 (IGFBP-7) to generate an AKI risk index (AKIRISK™ Score). Patients with an AKIRISK™ Score less than 0.30 are at low risk of developing moderate to severe AKI within 12 hours of assessment while those with values ≥ 0.30 are at increased risk. We have evaluated the performance of the VITROS NEPHROCHECK Test on the VITROS 3600 Immunodiagnostic System and the VITROS 5600 Integrated System. The test is linear across the range of 0.4 to 29.7 ng/mL for TIMP-2; and 5.6 to 463.0 ng/mL for IGFBP-7 resulting in an AKIRISK™ Score range of 0.002 to 13.8. Limits of Blank were determined to be 0.164 ng/mL and 0.456 ng/mL for TIMP-2 and IGFBP-7, respectively. Limits of Quantitation were determined to be 0.392 ng/mL for TIMP-2 and 1.393 ng/mL for IGFBP-7 respectively, resulting in an AKIRISK Score of 0.002. A 20-day precision study with pooled patient samples at mean AKIRISK Scores of 0.10, 0.32, 0.38, 2.24, 3.46, 6.72, and 8.16 resulted in within-laboratory percent coefficients of variation (%CV) of 10.9%, 10.6%, 12.3%, 11.3%, 8.7%, 6.9% and 6.9% respectively on the VITROS 3600 Immunodiagnostic System. Similar results were obtained from the VITROS 5600 Integrated System. Potential endogenous interfering substances likely to be present in urine including acetoacetate, acetone, ammonia, albumin, creatinine, hemoglobin, myoglobin, urea and uric acid were tested and shown not to interfere in the assay. The accuracy of the test was evaluated with 145 patient specimens spanning the assay measuring

range against the Astute Medical NEPHROCHECK Test System (Astute) and the following linear regression statistics were obtained: VITROS 3600 = 1.07*Astute + 0.03; (r) = 0.96; and VITROS 5600 = 1.03*Astute + 0.05; (r) = 0.96. Studies were performed to determine the clinical utility of the VITROS NEPHROCHECK Test using samples (n=339) collected from the intended use population and healthy cohorts (n=399). VITROS results were assessed based on AKIRisk Score of 0.30 against clinical outcome. Presence or absence of acute kidney injury was determined by clinical adjudication. A sensitivity of 87.27% (95% exact confidence interval: 75.52% to 94.73%) and specificity of 49.30% (95% exact confidence interval: 43.34% to 55.27%) with a negative predictive value of 95.24% (95% exact confidence interval: 90.43% to 98.06%). The assay demonstrated good performance and showed high negative predictive value indicating utility in identifying patients at risk of developing acute kidney injury within 12 hours of assessment. (* under development)

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Alkaline phosphatase reference interval in children and adolescents in Brazil

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Background: The interpretation of laboratory tests requires reference intervals (RI) that may vary between different populations. For the diagnosis of hypophosphatasia, disease presenting with low serum alkaline phosphatase (ALP), lower limits of RI must be well determined. Since the ALP methodology in practice in our clinical laboratory does not provide lower reference levels for children and adolescents, our aim was to validate lower limits through CALIPER findings, adjusted to the Brazilian population. **Methods:** Serum specimens of 1950 children, from 1 to 18 years old, reporting ALP measurement, between April 2015 and March 2016, were retrospectively assessed. The same subgroups proposed by CALIPER study and the Clinical and Laboratory Standards Institute (CLSI) guideline have been used to validate obtained results. ALP was measured by the Roche/Hitachi platform Cobas. Inclusion criteria were patients with normal results for liver function, bone metabolism, kidney function, and blood counts. Exclusion criteria were hospitalization, low weight, use of drugs that could interfere in the ALP measurement, and patients in which ALP dosing was requested more than 3 times. The percentage of girls and boys excluded were 13,9% and 12,8%, respectively, therefore 1690 patients were selected. Data normal distribution was analyzed with Kolmogorov-Smirnov test. Outlying observations were calculated using Dixon test. RI was defined as 2.5-97.5%. The RI obtained in this study was considered valid if less than 10% of patients were out of CALIPER RI, and if the difference between minimum and maximum value for each age group and sex was less than 25% between both studies. **Results:** The obtained RI results and 90% confidence interval (CI) of ALP are shown in Table 1. **Conclusion**: According to CLSI, the results of this study have been enabled for use as ALP RI when compared to CALIPER study, for the Brazilian children and adolescents' population.

Table 1- Data of patients selected, and results of Brazilian study compared to CALIPER study.

Age group (years)	Gender group (n)	Total number of patients (n)	Patients excluded (n/%)	Patients selected (n)	ALP RI (U/L)	ALP CI	Outsiders (n/%)	CALIPER RI (U/L)	Difference* (%)
1-9	Both	322	32/11.3	282	149-301	(134-319)	24/7.45	135-320	+10.0/-6.0
10-12	Both	232	24/11.5	208	127-326	(122-401)	19/8.1	122-400	+4.0/-18.5
13-14	Girls	199	26/13.0	173	62-212	(51-246)	4/2.0	52-243	+19.1/-12.7
13-14	Boys	197	12/6.0	185	129-437	(101-454)	18/9.1	109-449	+18.3/-12.7
15-16	Girls	248	33/13.3	215	52-120	(45-122)	24/9.6	46-110	-11.5/+9
15-16	Boys	250	39/15.6	211	78-268	(62-334)	9/3.6	77-317	+1.3/-15.4
17-18	Girls	252	43/17	209	45-97	(40-99)	25/9.9	41-82	+9.7/+18.2
17-18	Boys	250	43/17.2	207	40-129	(38-141)	16/6.4	50-142	-9.1/-9.1

Legend: ALP: alkaline phosphatase; Patients selected: Total number of patients minus patients excluded; ALP RI: Reference interval for ALP determined in this study; CI: 90% confidence interval; Outsiders: number of subjects tested in the present study that fell out 10% above or below the original reported limits; RI: reference interval; * Percent difference to plus (+) or minus (-) the results obtained in this study compared to CALIPER study. The first percentage refers to the inferior reference value difference and the second value refers to superior reference value difference; CALIPER: Canadian Laboratory Initiative in Pediatric Reference Intervals.