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APPLICABILITY OF THE BIOMARKERS OF CHRONIC ALCOHOL ABUSE IN THE STRATEGIES TO IMPROVE TRAFFIC AND WORKPLACE SAFETY

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BACKGROUND-AIM

If the relationship between blood alcohol concentration (BAC) and road accident occurrence has extensively been studied, less attention has been devoted to the study of the "predictive value" of the biomarkers of chronic alcohol abuse. Aim of the present work was the investigation of the hypothesis of association of one or more of these biomarkers with the occurrence of traffic accidents, also among professional drivers.

METHODS

Subjects admitted to hospital for accident-related injuries (InjDr) (N= 468) were divided in two groups on the basis of the BAC (≤ 0.5 and > 0.5 mg/mL); a group of control subjects (drivers with no record of recent accidents, N=236) was also included. GGT and CDT in serum were determined in by using enzymatic analysis and HPLC, respectively.
EtG in hair was studied by using GC/QQQ-MS in cases of fatal road accidents (N= 60).
The association of the increase of these biomarkers with the occurrence of alcohol related traffic accidents (i.e. with BAC > 0.5 mg/mL) was verified by using statistical methods.
CDT analysis was also applied to check the fitness-to-work in a group of professional bus drivers (n=503).

RESULTS

Using a cut-off of 1.9%, 36 of 100 InjDr with BAC > 0.5 g/L, showed elevated CDT. Comparing this subgroup with the control group (CDT positives 0.4%), the Odds ratio was as high as 132, with a p value well below the 0.001 threshold (Fisher's test).
On the other hand, only 7 out of 368 InjDr with BAC ≤ 0.5 g/L (1.9%) showed elevated CDT concentrations, resulting not significantly different from the control group (Odds ratio).
GGT proved also significantly elevated in the InjDr, but with a lower degree of statistical significance in comparison with CDT.
Finally, EtG in hair was found increased in 44% of the alcohol related traffic fatalities (cut-off 30 pg/mg), but also in 17% of the non-alcohol related accidents.
The application of CDT analysis in the assessment of the fittness-to-work of professional drivers showed a low but not negligible prevalence of alcohol abusers (about 2%), which were directed towards psychological counselling with rapid normalization of the CDT values.

CONCLUSION

The use of CDT for the assessment of the fitness to drive is objectively justified. GGT and EtG show a promising potential in this field.
The use of biomarkers of chronic alcohol abuse, and particularly CDT, has proved also useful in the assessment of the fitness-to-work in case of safety sensitive jobs.

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ASSESSMENT OF PROTEINURIA BY USING PROTEIN CREATININE RATIO IN SPOT URINE SAMPLE VERSUS 24 HOURS URINE SAMPLE

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BACKGROUND-AIM

Assessment of proteinuria is used as a diagnostic as well as a prognostic marker for kidney disease. 24 hours urinary protein is a gold standard method to assess proteinuria but collection of 24 hours urine is time consuming, and despite of proper instruction to patients, there may be inevitable chances of error during collection of 24 hours urine sample or inaccuracy in the timing of collection. Various research works have been conducted in different clinical conditions of proteinuria to find out correlation between protein creatinine ratio (PCR) in spot urine and 24 hours urinary protein (24HUP). All of the studies have reported varying degree of positive correlation and established different PCR value for different cutoff of 24 hours urinary protein a standard method for assessment of proteinuria. Our objective was to find the correlation of 24HUP and PCR in spot urine in our setup at various level of proteinuria irrespective of its cause and establish a cutoff PCR value at proteinuria ≥150mg/day.

METHODS

Sixty four patients with clinically suspected cases of proteinuria were recruited after convenient sampling method. 24 hours urine, spot urine and blood sample were collected after informed consent. Protein and creatinine were measured by Turbidimetric method and Jaffé method respectively by Roche chemistry auto analyzer, (cobas c 311) at biochemistry laboratory.

RESULTS

A good positive correlation (Spearman's correlation r=0.70, P<0.0001) was observed between 24HUP and PCR in spot urine. The value of Spearman's correlation was relatively higher at proteinuria ≥150mg/day as compared to <150mg/day. The area under the ROC curve for PCR in spot urine at various cutoffs is 0.85 (95.0% CI; 0.75-0.95 p <0.0001). A sensitivity of 83.9% and specificity of 75.8% were achieved to detect proteinuria ≥150mg/day at the PCR cutoff greater than 0.20. With this cutoff, the positive predictive value was found 76.5% and negative predictive value was found 83.3%.

CONCLUSION

We observed a good positive correlation between 24HUP and PCR in spot urine and PCR value ≥0.20 represented proteinuria ≥150mg/day.

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THE EVIDENCE OF CLINICAL AND COST EFFECTIVENESS OF USING MALDI-TOF MASS SPECTROMETRY FOR BACTERIAL IDENTIFICATION

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BACKGROUND-AIM

Identification of bacterial species is necessary for diagnosis and efficient treatment. Recent reports indicate that Matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI-TOF MS), which provides a unique mass spectral fingerprint of microorganisms, may be more successful in indentifying bacteria and yeasts than standard biomedical tests. In light of these concerns, the purposes of this study is to exam and ascertain the effect of using MALDI-TOF MS as compared to the conventional biochemical tests in identifying bacterial strains.

METHODS

A literature search was conducted on key resources. The literature search yielded 450 citations. Abstracts were reviewed and those indicating a comparative evaluation between MALDI-TOF MS and biochemical testing of bacteria identification were selected. Thirty-six comparative studies were identified and retrieved for further screening and final selection. Studies that cannot download full contents, studies that did not clearly state the comparator, or studies that chose one species bacteria as subjects, were excluded. All total of four cross-sectional studies were included and appraised in this report.

RESULTS

Four studies identified in this article indicate that MALDI-TOF has shorter turnaround times, less costly and better diagnostic accuracy than conventional biomedical tests. To confirm the advantage of MALDI-TOF MS described in literature. Our laboratory also used a wide range of species of bacteria to evaluate the performance of MALDI-TOF MS technology. The average identification turnaround time of MALDI-TOF MS was saved 28.4 h. The MALDI-TOF MS also save 950,000 NTD per isolate identification and 165,000 NTD waste-clean costs. 354 isolates identified by MALDI-TOF had good concordance with conventional biomedical tests, with >94.6% correctly identified to the species level.

CONCLUSION

Above evidence indicate that MALDI-TOF MS has important implications for patient care and health care costs, as this technology can potentially impact the speed and accuracy with which infective bacteria are identified and correctly treated.

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DOES PLASMA NGAL HELP FOR PREDICTION OF ACUTE KIDNEY INJURY IN SEPSIS PATIENTS? : A SYSTEMATIC REVIEW AND META-ANALYSIS

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BACKGROUND-AIM

It is well known that neutrophil gelatinase-associated lipocalin (NGAL) is a useful biomarker for the early diagnosis of acute kidney injury (AKI) in general population; however, it can be elevated in patients with sepsis as well. So, the diagnostic value of NGAL for predicting AKI in sepsis patients is uncertain. We aimed to evaluate the diagnostic value of plasma and urine NGAL to predict AKI in sepsis patients.

METHODS

MEDLINE, EMBASE, and Cochrane Library were searched for articles evaluating the predictive value of plasma and/or urine NGAL for AKI in sepsis patients. Two Authors independently extracted data including study characteristics, NGAL assay method, and type of specimen.

RESULTS

Thirteen studies from 9 countries with a total of 1592 (range of 11 to 661 for each study) patients, of whom 329 (20.7%) developed AKI, were included: 12 studies evaluated blood NGAL (9 plasma and 3 serum) and 5 studies evaluated urine NGAL. All included studies except one were prospective observational cohort studies. Diagnostic criteria of sepsis and AKI in adults patients were SCCM criteria and RIFLE/AKIN criteria, respectively, but diagnostic criteria of sepsis and AKI in neonate/pediatric patients were varies among studies. Plasma NGAL of adult sepsis patients with AKI were significantly higher than those without AKI (mean difference 274.7 (95% CI, 106.16-443.15), I^2=94%, P=0.001). Plasma NGAL of pediatric sepsis patients with and without AKI was not significantly different between two groups. Urine NGAL of adult and pediatric patients with and without AKI was not was not significantly different between two groups. Using a hierarchical bivariate generalized linear model to calculate the diagnostic odds ratio (DOR) were calculated. DOR of plasma NGAL to predict AKI in sepsis patients was 6.64 (95% CI, 3.80-11.58). Diagnostic accuracy of plasma NGAL was 0.881 (95% CI, 0.819-0.923) for sensitivity and 0.474 (95% CI, 0.367-0.582) for specificity.

CONCLUSION

Plasma NGAL level was a useful early diagnostic marker for predicting AKI in the adult sepsis patients.

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USE OF PROCALCITONIN IN THE ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN THE EMERGENCY ROOM : A COSTS/BENEFITS AND HOSPITAL PRACTICE SHORT STUDY

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BACKGROUND-AIM

Utility of procalcitonin (PCT), a marker allowing early detection of bacterial infection, in acute exacerbation of COPD (AECOPD) was evaluated in our emergency room (ER). Influence of PCT results on antibiotics prescription and treatment duration, as well as costs/benefits ratio, were addressed.

METHODS

PCT analyses were performed stat on a Mini-Vidas (Bio-Mérieux). ER physicians were asked to complete a survey and to rely on an adaptation of a published algorithm. Follow-ups of hospitalized patients were managed by family physicians. PCT data and surveys were analysed.

RESULTS

33/45 (73%) PCT measurements were adequate. Of those, 29 had a well completed survey. Four hospitalized patients were also included in the study even though not consulting initially at the ER. Procalcitonin results guided decision to prescribe antibiotics (or not) in 70% of the cases. Consequently, 61% of patients (20/33) did not receive antibiotics following a negative PCT result. However, once antibiotics were initiated, subsequent negative PCT measurements had little effect on reduction of treatment duration (11% of hospitalized patients, and 15% upon discharge). The costs/benefits ratio was poor. Savings on antibiotics represented only 18% of costs generated by PCT analyses.

CONCLUSION

Although not cost-effective in the short term, the use of PCT could lead to significant long term benefits and savings through the reduction of antibiotics prescription, which could ultimately lead to a reduction in cases of Clostridium difficile infection and antibiotic's resistance in our community.

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FROM UNCOMPENSATED JAFFé TO CROATIAN NATIONAL GUIDELINES FOR LABORATORY DIAGNOSTICS OF CHRONIC KIDNEY DISEASE (CKD) – THE INITIAL PHASE

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BACKGROUND-AIM

In February 2014 a new Joint Working Group (JWG) of Croatian Society of Medical Biochemistry and Laboratory Medicine (CSMBLM) and Croatian Chamber of Medical Biochemists (CCMB) for laboratory diagnostics of CKD was established. The final aim of the JWG is to provide first Croatian guidelines for laboratory diagnostics of CKD.

METHODS

At the initial meeting of the JWG a detailed workflow was developed. It conforms to the regulations of the CSMBLM Committee for Scientific and Professional Development and comprises following steps:
1. Assess the current state of laboratory diagnostics of CKD in Croatian medical biochemistry laboratories.
2. Prepare initial concept of recommendations for laboratory diagnostics of CKD.
3. Apply the text of the recommendations for the peer-review process in indexed scientific Journal with an international review process.
4. After the completion of the international peer-review process prepare the text of recommendations in Croatian language.
5. Provide extensive support in implementation process in a form of lectures and webinars.
6. Follow-up after implementation of the guidelines.

RESULTS

In 2014 members of the JWG accomplished the first 2 predefined goals:
1. To assess the current state of laboratory diagnostics of CKD in Croatian medical biochemistry laboratories an on-line survey was conducted from March till May 2014. The survey results showed large heterogeneity in this area of laboratory medicine and supported the need for national guidelines.
2. In September 2014 the Chair of the JWG gave a lecture in a form of webinar for the members of CSMBLM. The presented topic was introduction into the new Kidney Disease: Improving Global Outcomes (KDIGO) 2012 guidelines and initial survey results.
3. The collected survey results were prepared as the Original article titled „Laboratory diagnostics of chronic kidney disease in Croatia: state of the art„ and on January 3rd 2015 accepted for publication in Biochemia Medica Journal.
4. The initial draft of the guidelines for laboratory diagnostics of CKD in Croatia was finished in January 2015.

CONCLUSION

The background for the first Croatian guidelines for laboratory testing of CKD was set in 2014. In 2015 the main goal is to provide the guidelines and to give support for the implementation process.

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URINE SEDIMENT EXAMINATION: A COMPARISON AMONG 3 AUTOMATED URINANALYSIS SYSTEMS AND 2 MANUAL MICROSCOPY (STAINED AND NON-STAINED) METHODS

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BACKGROUND-AIM

Urinalysis is one of the most commonly used in vitro diagnostic screening tests in clinical practice for detecting systemic diseases. Our aim was to investigate and compare urine sediment examination results from Aution Hybrid AU-4050 (ARKRAY Global Business Inc., Kyoto, JAPAN), Fus-200 (DIRUI Industrial Co., Changchun, China) and US2012A(BIOBAK A.S., İstanbul, Turkey) as well as manual microscopic evaluation of stained (with Crystal Violet) and non-stained slides.

METHODS

We studied 292 freshly collected urine specimens submitted for diagnostic urinalysis to our laboratory at the hospital of Kocaeli University, Faculty of Medicine. We examined and correlated the following in HPF (high power field): Red Blood Cells (RBCs), White Blood Cells (WBCs), Bacteria, Yeast, Crystal, Epithelial cells and Casts. Statistical analysis was performed using IBM SPSS 20.0 ($p<0,05$ was considered statistically significant).

RESULTS

When compared with other methods, significantly higher RBC counts have been identified with US2012A device. ($p<0,001$). Aution Hybrid, using flow cytometric method, detected higher WBC counts than US2012A ($p<0,01$) as well as the other methods ($p<0,001$). Moreover, Aution Hybrid detected the highest bacteria count ($p<0,001$). Significantly higher epithelial counts were yielded by US2012A when compared to Aution Hybrid and Fus-200 ($P<0,001$). No statistically significant difference was found between methods for yeast identification. Although there was no significant difference between methods in detecting cast, Aution Hybrid was found to have the best detection power ($p=0,001$). When compared with the other methods, non-strained microscopic method detected greater number of crystal and the results were statistically significant ($p<0,05$)

CONCLUSION

Although manual method is clinically useful, it's also full of methodological problems. It's labor-intensive, time-consuming, imprecise and has wide interobserver variability. For these reasons, automated methods are better than the manual method. But when evaluated in terms of all parameters, there is no superiority between the automated methods.

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DECREASED FIBRINOGEN AND ALBUMIN LEVELS IN PREDICTING MORTALITY OF HOSPITALIZED MEDICALLY ILL PATIENTS

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BACKGROUND-AIM

In determining the risks of probable morbidity and mortality at earlier period is for the management and multidisciplinary follow up of the patients, we aimed to evaluate the impact of plasma levels of fibrinogen, serum levels of albumin, age, smoking, sex, hospital accommodation section as well as the Eastern Cooperative Oncology Group (ECOG) performance status and Charlson comorbidity index (CCI) on the survival of hospitalized medically ill patients at discharge and at 6 months of follow-up.

METHODS

A total of 313 patients (139 females, 174 males) aged 18 – 99 and having CCI scores ≥2, ECOG scores ≥1 included the study. It was noted that if the patients were alive or dead at the time of discharge from hospital and also at the end of 6 months. Plasma fibrinogen levels were measured by Clauss method on CA 1500, and serum albumin levels were measured by bromocresol green method on Advia 2400 (Siemens Healthcare Diagnostics).

RESULTS

At admittance to the hospital, the mean values of age, CCI scores, ECOG scores, fibrinogen levels and albumin levels were as follows; 67.8±13.9, 5.0±2.4, 2.4±1.1, 416.8±155.7 mg/dL, 3.5±0.6 g/dL, respectively. In-hospital mortality rate was 18.5%. Total mortality rate at the end of 6 months follow-up was 47.9 %. Factors that affect the risk of in-hospital mortality were analyzed with the logistic regression analysis backward method, decreases in fibrinogen (OR=0.997, 95 % CI, 0.995 – 0.999, p=0.008) and albumin (OR=0.532, 95 % CI, 0.298 – 0.949, p=0.033) were statistically significant risk factors. Factors that affect the mortality during 6 months follow up were also analyzed with cox regression analysis backward method, decreases in fibrinogen (OR=0.998, 95 % CI, 0.997 – 0.999, p=0.001) and albumin (OR=0.574, 95 % CI, 0.434 – 0.760, p<0.001) were significant risk factors.

CONCLUSION

Laboratory parameters of fibrinogen and albumin were evaluated together with other factors and clinical scores to predict mortality for in-hospital patients or for patients after discharge, and decreased levels of them appeared to be statistically significant risk factors. In post-analytical phase, utilization of laboratory test results through mathematical models with other clinical data should bring more benefits.

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UTILITY OF CALCULATED GLOBULIN FRACTION AS A SCREENING TOOL FOR THE DETECTION OF MONOCLONAL GAMMOPATHIES.

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BACKGROUND-AIM

The use of arbitrary cut-offs for calculated globulin (cG), estimated as the difference between total protein and albumin, has been reported to identify immunoglobulin (Ig) deficiency and monoclonal gammopathy with a variable success. Utility of this approach, however, has not been fully characterized. We undertook a retrospective study to examine the diagnostic performance of cG in a cohort of patients suspected of monoclonal gammopathy.

METHODS

Of 229,000 consecutive serum protein electrophoresis (SPE) results over ~3.5 years, 3974 had immunofixation electrophoresis (IFE) requested and performed concurrently. Total protein, albumin (part of SPE) and Ig concentrations (part of IFE) were determined on the Roche Modular E170, while SPE and IFE were performed on the Sebia Capillarys™ II and Hydrasys™ systems respectively. Reference intervals (RI) (2.5th-97.5th centile) of cG were determined on 1800 individuals with normal serum proteins, IFE and Ig levels. Sensitivity, specificity, positive (PPV) and negative predictive values (NPV), and odds ratios (OR) were determined using GraphPad InStat v3.01.

RESULTS

The RI of cG was 19-33 g/L. cG>33 predicted at least one Ig (out of IgG, A and M) increase with sensitivity 0.36, specificity 0.98, PPV 0.93 and NPV 0.73, while cG<19 predicted at least one Ig reduction with sensitivity 0.15, specificity 0.99, PPV 0.86 and NPV 0.74. As to the detection of monoclonal gammopathy, 54/195 (27.7%) and 314/556 (56.5%) were tested IFE positive among those with cG<19 and cG>33 g/L respectively. Taken together, an abnormal cG (< 19 or >33 g/L) yielded sensitivity 0.29, specificity 0.86, PPV 0.49, NPV 0.72 and OR 2.48 (95% CI: 2.11-2.91) for M-proteins. Aggressive M-protein isotypes (non-IgG and free light chains) were more common among cG<19 than cG>33 group (50% Vs 35.7%).

CONCLUSION

The high specificity and above-average NPV suggest that cG<19 may be used to rule out rather than to rule in Ig deficiency. While the odds of finding an M-protein among those with an abnormal cG is significantly higher, the poor sensitivity (0.29) and mediocre PPV (0.49) do not qualify it as an effective screening test. Additional modifiers that will improve the diagnostic performance are recommended when using cG as a screening tool.

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DIFFERENCES IN LEVELS OF BIOMARKERS IN HEALTHY AND FRAIL ELDERLY.

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BACKGROUND-AIM

Ageing is related to a decline in vital physical functions in elderly individuals. An issue is to determine whether a change is ascribable to ageing alone, independent of disease processes. When assessing the presence of disease, physicians rely on reference intervals provided by the laboratory. Current reference values, though, are based apparently healthy subjects in the ages 18-65 years. Recently, we reported that nursing home residents (NHR) differ in values of common biomarkers compared with values from current reference populations. The aim of the present study was to investigate if there are differences between levels of common biomarkers in healthy elderly individuals compared to frail elderly individuals.

METHODS

The sample consisted of 138 frail NHR, mean age 86,8 years. Common conditions were chronic heart disease (68 %), dementia (28%) and stroke (24%). From the Nordic reference project (NORIP), 64 healthy individuals, 80 years and older, with no medication were included as healthy elderly in this study. From The Elderly in Linköping Screening Assessment (ELSA-85) study, 329 vital elderly at the age of 85 years living in their own accommodations, were included. Some diseases occur among these individuals, but they are much more vital than NHR. Venous blood were collected in evacuated tubes with EDTA and LiH as anticoagulant, centrifuged and frozen in -70°C until analysed. Alanine aminotransferase (ALT), albumin, aspartate aminotransferase (AST), creatinine, gamma-glutamyl transferase (γ-GT) and sodium were analysed by accredited routine laboratory assays. T-test was used to compare means between groups.

RESULTS

NHR had significantly lower mean levels of AST, ALT, sodium and albumin compared to both ELSA ($p<0.05$) and NORIP ($p<0.01$). For γ-GT, ELSA had the highest mean level (0.59 µkat/L+0.58), while NORIP had the lowest (0.43 µkat/L+0.17). For creatinine NHR had the highest level (107 mmol/L+31), while NORIP had the lowest (80 mmol/L+16).

CONCLUSION

The study shows the importance of being aware of different reference populations in relationship to expected outcome of laboratory tests, when assessing the individual patient. Otherwise there is a risk of misjudging the presence as well as absence of disease, especially in frail NHR.

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APPROPRIATENESS OF TUMOR MARKER (TM) ORDERING AFTER APPLICATION OF LOCAL GUIDELINES (LG): DO NOT LOOSE THE CONTROL

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BACKGROUND-AIM

In 2006 we introduced in our academic medical center LG for correct TM use. As a general rule, we established a maximum of two TM requests in the same order except for well documented clinical situations. In this study, we evaluated the level of inappropriateness of TM ordering, which is persisting 6 years after the introduction of LG, and we investigated the main factors potentially influencing clinicians when performing an inappropriate TM request. For this purpose, we referred to a consecutive case series of requests from hospital wards exceeding two TM, prospectively identified from Sept 2012 to May 2014.

METHODS

TM requests were identified as potentially not compliant to LG by an ad-hoc electronic database and immediately discussed with the clinical requestor contacted by phone by laboratory specialists. The clinician reviewed the ordering and declared the reason supporting the request. From corresponding clinical records, we retrieved patients' features, additional diagnostic tests and diagnosis at hospital admission and discharge.

RESULTS

A total of 104 out of 2860 requests (3.6%) were automatically blocked. Several of those were performed for diagnostic purpose. The most frequent as well as inappropriately requested TM were CEA and CA 19.9. The inappropriateness of requests appeared to be linked to the need of more education and knowledge on their clinical applicability and limitations. The clinical motivation was generally associated to patients: a) carrying non-specific signs/symptoms (i.e., weight loss with worsening general conditions), b) resulting incidentally positive to some recently performed TM tests, or c) being tested by TM to avoid more expensive diagnostic imaging procedures. According to multiple regression models there was no evidence that increases in patients' age as well as in AST, ALT, LDH or CRP concentrations in plasma might have influenced clinicians in requiring more or inappropriate TM.

CONCLUSION

We have shown that the solely release of LG to guide TM ordering is not enough to curb the excess of requests and maintain the appropriateness, but this should be supported by a strict monitoring on a daily basis by laboratory professionals as well as a continuous consultation with requesting clinicians.

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ESTIMATION OF SIGNIFICANT-LEVELS OF INTRA-INDIVIDUAL VARIATIONS FOR COMMON LABORATORY TESTS FROM A LONG-TERM HEALTH SCREENING DATABASE.

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BACKGROUND-AIM

In 2008, Japan Health Ministry implemented a health promotion scheme for reducing life-style related diseases such as metabolic syndrome (MetS). Therefore, it is important to have objective criteria to judge the level of improvement. Conventionally, the magnitude of intra-individual variations is expressed as CV (CV_I), and reference change value (RCV) has been proposed as a 95%CI of difference between any two measurements. However, RCV assumes Gaussian distributions of test results and constant CV over the range of values for healthy individuals. In this study, level-specific intra-individual variations were evaluated from a large-scale, long-term health screening database recorded over the past 14 years, and critical levels of intra-individual changes were estimated in reference to a new index representing the severity of MetS.

METHODS

Level-specific RCV were estimated (for glucose, HbA1c, TG, HDL-C, LDL-C, ALT, and GGT) from the database of 9,500 health screening attendees recorded in Dept of Health Screening, Jikei Univ Hospital, Japan. Exclusion of individuals under medication or with a large change in BMI led to reduction of data size to 6,121. Metabolic index (MetI) was derived by logistic regression analysis by setting age, BMI, DBP, SBP, TG, HDL-C, and glucose as explanatory variables from a dataset composes of 1,500 and 15,000 cases with or without MetS. Critical level of change in a given test were estimated as 80% improvement in MetI.

RESULTS

Test level dependency of CV_I was apparent for TG, AST, ALT, and GGT and amendment of RCV using the CV_I is essential for proper application of CV_I. The logistic regression analysis gave excellent separation (area under ROC curve of 0.89) of subjects with or without MetS. As a typical result, the level of delta changes which corresponded to 80% changes in MetI were 11 U/L for ALT, 40 mg/dL for TG. A diagram of level specific CV_I (test level on x-axis; CV_I on y-axis) revealed that the estimated significant level of changes for each test item corresponded to approximately $1.6CV_I$ to $1.8CV_I$.

CONCLUSION

The estimated level of intra-individual change which match significant change in MetI was significantly lower than that specified by RCV. It appears appropriate to modify RCV by computing 80% rather than 95% CI of intra-individual variations.

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THE UK NATIONAL MINIMUM RE-TESTING INTERVALS IN PATHOLOGY PROJECT

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BACKGROUND-AIM

Over the last 10 years, Pathology workload in the UK has seen an average annual increase of 10% accompanied by increasing costs and reduced revenues. The laboratory needs to identify appropriate and inappropriate requests to ensure the right test is done on the right patient at the right time. Demand management solutions continue to be developed to address this need using a variety of tools supported by appropriate evidence, where available and partnership working. Minimal re-testing intervals (MRI) are defined as the minimum time before a test should be repeated, based on the properties of the test and the clinical situation in which it is used. The National MRI Project delivered a set of recommendations aimed at addressing the lack of consensus and evidence based guidance for use of MRIs in Primary and Secondary care in Clinical Biochemistry testing. The aim of this project was to produce recommendations for all areas of pathology.

METHODS

Recommendations were prepared by members from each of the Royal College of Pathologist's discipline specific Specialist Advisory Committees investigating evidence and existing guidelines to prepare recommendations. The method used to prepare these recommendations was termed 'the state of the art', the same approach used in the original MRI project. Where no evidence-based guidance existed either in the literature or published guidance, recommendations were prepared based on the consensus opinion of the working group. The final document was then sent out for final consultation to invited members of the Royal College of Pathologists.

RESULTS

373 recommendations were prepared in the following disciplines: Clinical Biochemistry (134), Haematology (41), Immunology (100), Microbiology (63), Virology (23) and Cellular Pathology (12).

CONCLUSION

Using a collaborative approach the working groups of the MRI in Pathology project have prepared a number of consensus based recommendations that can be used across all areas of pathology. These recommendations will support the National Laboratory Medicine Catalogue and National Demand Management Toolkit for Pathology (NDMTP).

Evidence-based medicine, Lab medicine practice guidelines, decision making

M404

IRRATIONAL USE OF LABORATORY TESTS AT PRIMARY HEALTHCARE LEVEL

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BACKGROUND-AIM

Laboratory tests can only be valuable if rationally used. Rational use means right test for right patient at right time. Unfortunately, in routine laboratory practice we have high rate of unnecessary tests performing, without respecting national and international guidelines and without clear idea how results will be used in further patient management. Possible causes for this situation could be: ignorance of tests' characteristics and their clinical utility, availability of large number of different laboratory tests, patient's pressure on the doctor and doctor's fear of potential lawsuits.
Aim of this paper is to show current situation in our laboratory concerning number of tests ordered per request and their compatibilty with diagnosis.

METHODS

Data were extracted from laboratory information system about number and kind of tests per request and about diagnosis in our laboratory during 2014.

RESULTS

Average number of tests per request is 14, going from 1 to 34. There are some illustrative examples of irrational use of laboratory tests. We have done 1298 analysis of amylase but only 150 requests were with diagnosis of pancreatic disease. 1113 patients which were sent to our laboratory for the first time thyroid function evaluation during their routine health check had simultaneously ordered FT4 although in 92 % their TSH value was within reference range.

CONCLUSION

The number of requested tests in our laboratory is too high. Also frequency of repeating some tests is irrational. Requested tests are often in conflict with the guidelines for that diagnosis. Corrective measures should be: additional education for primary health care doctors, insisting on evidence based medicine, activity of national professional organizations in making laboratory diagnostic algorithms for different disease, good communication between clinicians and clinical biochemist, distributing written material about tests characteristics by laboratory, making more intuitive order forms for doctors, periodical reports to the management of institution about number of ordered tests per each doctor. Unnecessary testing makes time loss and financial costs to the laboratory and provides no benefit for the patients or clinical decision making.

Evidence-based medicine, Lab medicine practice guidelines, decision making

M405

PROGNOSTIC AND MEDICAL RELEVANCE OF BONE TURNOVER MARKERS FOR MULTIPLE MYELOMA PATIENTS: AN EVIDENCE BASED APPROACH FOR CLINICAL LABORATORY

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BACKGROUND-AIM

Bone turnover markers (BTMs) may represent a non-invasive method to assess the bone involvement and to predict the risk of bone morbidity in patients with Multiple Myeloma (MM). We conducted a methodological investigation to evaluate the prognostic role of BTMs markers in MM patients using the technique of systematic review.

METHODS

We searched Medline and Embase. Results about C- and N-terminal telopeptide type I collagen (PICP,PINP), osteocalcin (OC), bone alkaline phosphatase (BAP), C- and N-terminal cross-linking telopeptide type I collagen (CTX, NTX), C-terminal cross-linked telopeptide type I collagen (ICTP), tumor necrosis factor related activation induced cytochine (RANKL) and osteoprotegerin (OPG) were extracted. The risk of bias was evaluated by the QUIPS checklist. Hazard ratios (HR) and 95% confidence intervals for each study were extracted and pooled with a random effects model. Heterogeneity and the meta-regression analyses were done.

RESULTS

We included 30 studies and more than 2500 patients. The majority of studies used ELISA, 10 studies used RIA. In MM patients, the concentration of reabsorption markers (NTX and ICTP) increased, instead the concentrations of formation markers (BAP and OC) reduced. High levels of ICTP were predictive of bone events (HR 1.18) and they were associated with poor survival (HR 1.08). NTX, instead, correlated with progression disease (HR 1.02). Within-studies heterogeneity was high. Most of the included studies were considered to be at high risk of bias. The incomplete reporting of characteristic of participant, methodology and results, explained the differences between studies.

CONCLUSION

BTMs may be clinically informative predictive biomarkers in the MM patients. The lack of method standardization explains the poor implementation in clinical practice. Further high-quality trials are needed to conclusively establish the utility of markers measurements.

Evidence-based medicine, Lab medicine practice guidelines, decision making

M406

CLINICAL IMPLICATION OF BODY MASS INDEX AND RELATED SYSTEMIC INFLAMMATION MARKERS IN THE SURVIVAL PREDICTION OF THE PATIENTS WITH SOLID TUMORS

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BACKGROUND-AIM

Emerging evidence on body composition suggests that sarcopenia that related with low body weight is one of the predictive markers of mortality in the patients with malignancy. Although sarcopenia could be determined with CT scan, body mass index(BMI) would be simply calculated with height and weight from the patient. We aimed to assess the relation between BMI and sarcopenia, and evaluate the systemic inflammatory markers could be prognostic values.

METHODS

Between Oct, 2012, and Sep, 2013, 78 patients with solid cancers were identified. Available CT images were analysed to determine sarcopenia. BMI were defined as normal weight (18.5-22.9 kg/m2), overweight (23.0-24.0 kg/m2), and obese (≥ 30 kg/m2). Clical data before the first cycle of chemotherapy were obtained. Kaplan-Meier analysis was applied to assess the BMI affecting overall survival (OS). Age, gender, performance status (PS), TNM stage, WBC, hemoglobin, platelet (PLT), neutrophil to lymphocyte (N/L) ratio, albumin, CRP, LDH were included for univariate and multivariate analysis. p value of <0.05 were selected for statistical significance.

RESULTS

In the study patients, male was 48, 61.5% and median age was 73 (range 65-91). The most common cancer site was lower gastrointestinal tract (n=14, 17.9%). 35% of patients were in sarcopenia, the median OS was 4.0 months (95% CI, 0.0-8.9) and 65% were in non-sarcopenia, the median OS was 10.3 months (95% CI, 7.6-12.6, p=0.040). In the results of BMI, 47.4% were normal weight, 48.8% were overweight and obese. Median OS was 7.6 months (95% CI, 6.1-9.0) in normal weight group, however, OS was significantly prolonged in higher BMI group with 12.7 months (95% CI, 5.7-19.6, p=0.047). In the multiple regression analysis, non-sarcopenia was associated with higher BMI (p=0.001), and the lower PLT count showed statistically significance with higher BMI (p=0.001) in the analysis of systemic inflammatory markers. CPR ≥ 7 (p=0.041), N/L ratio > 3 (p=0.026), albumin < 3 (p=0.017) were related with poor prognostic factors in survival analysis.

CONCLUSION

This study provides evidence of the BMI ranges and PLT counts in patients with cancer links body composition, especially sarcopenia that indicates declined survival curve. The systemic inflammatory responses are clearly implicated poor prognostic outcome in the study population. Further prospective study is required to validate the use of BMI and PLT count as a prognostic indicators in patients with newly diagnosed malignant disease.

Evidence-based medicine, Lab medicine practice guidelines, decision making

M407

ADDING VALUE TO VITAMIN B12 TEST UTILIZATION: FROM THE REQUEST TO THE RESULT INTERPRETATION.

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BACKGROUND-AIM

A large percentage of total errors occur in test request and results utilization. The aim was to analyse the pattern of primary care of vitamin B12 test request, and severe deficit patient's detection. Also, to study if vitamin B12 low results were communicated, received and reviewed by General Practitioners (GPs), if appropriate decisions were taken regarding treatment instauration and monitoring, and if vitamin B12 levels were recovered.

METHODS

Laboratory requests are made electronically from the patient's electronic medical record (EMR) by the general GPs and reports sent automatically. From 1st January 2008 to 31th December 2014, vitamin B12 demand was studied. Through a laboratory information system (LIS) search, the patients with a result lower that 100 pg/ml were detected. In EMR was checked if results were communicated and received and if results reviewed (patients treated). Based in current guidelines, it was agreed with GPs that a "result interpreted correctly and taken the consequently action" was when patient received intramuscular treatment prescription before one month after phlebotomy. "Follow up appropriate" when test was reordered after one year (years 2008 to 2013).

RESULTS

Vitamin B12 demand and severe vitamin deficit cases increased along years.
The 197 studied patient's results were communicated and received (100%). 168 were reviewed (85%), and 128 (65%) were interpreted correctly and taken the consequently action.
In the first six years (2008-2013) 149 cases were detected. 92 (61.7%) of them were interpreted correctly and taken the consequently action. 70 (76%) had a second vitamin B12 test request in one year period, recovering 57 (81.4%) patients the values into the reference range (Vitamin B12 > 200 pg/mL)

CONCLUSION

The more cases detected as more tests were requested suggest the need to promote vitamin B12 primary care demand. A percentage of low vitamin B12 results were ignored by GPs. From the laboratory is possible to find out if laboratory data are used correctly. It is necessary to design interventions to better contribute to the diagnosis, monitoring and treatment of diseases.

Evidence-based medicine, Lab medicine practice guidelines, decision making

M408

DIAGNOSTIC CARRYOVER: IN AUTOMATIC URINE ANALYZERS

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BACKGROUND-AIM

Carryover is an important problem of automatic analyzers which use fixed reusable tips on pipetting steps in liquid-handling systems. Carryover leads to false positive test results. We aimed to find out if there is significant carryover effect on red blood cells (RBCs) which causes false-positive hematuria in automatic urine chemistry (DIRUI H-800) and sediment (DIRUI FUS-200) analyzers.

METHODS

Urine samples collected from the adults urine specimens which came to our clinical laboratory for urinalysis. 24 samples with gross hematuria selected as containing high RBC concentration and 48 samples which had negative result in dipstick and 0/hpf in microscopic examination selected as containing low RBC concentration. Samples which had negative result in dipstick and 0/hpf in microscopic examination, analyzed again after the samples with gross hematuria. The percentage of carryover was calculated with the formula (carryover% = 100 x (b1-b2) / (a2-b2)). Carryover effect within results, was analyzed with Wilcoxon test.

RESULTS

The percentage of carryover was very high (%67) in DIRUI H-800 urine chemistry analyzer with false-positive hematuria percentage was %91 for the first samples came after gross hematuria and %20 for the second samples. Carryover% of DIRUI FUS-200 urine sediment analyzer was found %0,4 with false-positive hematuria percentage was %87 for the first samples came after gross hematuria and %6 for the second samples. Within the results of the same samples, the first samples analyzed after gross hematuria had significantly higher ($p<0,001$) results than the second samples analyzed after gross hematuria in both analyzers.

CONCLUSION

In urine sediment analyzer, carryover% calculated with formula was found analytically sufficient, but it causes highly false-positive results because diagnostic limit of hematuria (RBC >3/hpf) is low. To prevent carryover in both urine analyzers; washing steps and procedures must be revised and biochemists must also pay attention to diagnostic carryover.

Evidence-based medicine, Lab medicine practice guidelines, decision making

M409

SHARP DECREASE IN PSA AND IN VITAMIN D PRESCRIPTIONS FOLLOWING THE INTRODUCTION OF EVIDENCE-BASED-PRESCRIPTION-FORMS.

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BACKGROUND-AIM

In France practice guidelines of the Haute Autorité de Santé (HAS) are not implemented as often as they should. As a consequence resources are wasted that be could be useful elsewhere.

METHODS

In Avril 2014 prescription-forms were introduced in our hospital for PSA and for vitamin-D. If those forms were not filled-in by the physicians, then PSA and vitamin-D were not measured any more by our laboratory. PSA was measured in only two circumstances: therapeutic follow-up of, or screening for, prostate cancer. Patients had to give their formal consent for being screened with PSA. Vitamin-D was measured in the only six circumstances recommended by the HAS.

RESULTS

After seven months of use of these two forms we observe a shatp decrease in PSA, and even more so in vitamin D, measurements (Table).
Table: number of vitamin-D and of PSA measurements over a 7-month-period, before and after the introduction of two prescription-forms in April 2014

	Vitamin-D	PSA
Avril – October 2014	231	348
Avril – October 2013	635	594
Avril – October 2012	537	636

CONCLUSION

Our prescripton-forms' legitimity is high because they are based on governmental guidelines. All the more since the values that are promoted in these guidelines clearly cover the four core principles of bioethics, that is beneficence, non-malevolence, respect for the patient's autonomy (particularly for PSA) and equity. Our results need to be comfirmed over a longer period of time, and be analysed in more detail, particularly regarding the way consent forms are filled-in by the patients.

Evidence-based medicine, Lab medicine practice guidelines, decision making

M410

FROM LABORATORY TO CLINICS: GUIDELINES FOR THYROID (DYS)FUNCTION TESTS - WE DID IT.....TOGETHER!

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BACKGROUND-AIM

Thyroid function tests, a very costly item for laboratory services, are often requested unjustifiably. Therefore, we have tried to implement the Croatian Thyroid Society Guidelines for rational detection of thyroid dysfunction (the Guidelines), developed in accordance with other thyroid international organizations, into the practice during last 5 years. Hereby we present the achievements of our activities expressed as compared numbers of the requests for thyroid function tests for in- and out-hospital patients for 2008 and 2013.

METHODS

During 5 years we have continuously presented the Guidelines to the hospital and general practice physicians via lectures, distribution of the Guidelines leaflets, posting of the Guidelines on hospital website, and daily-based personal contact with physicians. The numbers of requests of each thyroid test combination in 2008 and 2013 were analyzed and the results were expressed as percentages of total number of performed thyroid tests.

RESULTS

The laboratory of Zadar General Hospital received 21803 and 27187 requests for thyroid tests for in- and out-hospital patients in 2008 and 2013, respectively. The percentages of tests combinations recommended in the Guidelines were: 6.0% vs. 30.8% (TSH), 1.1% vs. 34.6% (TSH+T4), 2.0% vs. 21.3% (TSH+FT4), while of unjustified combinations 79.3% vs. 3.3% (TSH+T3+T4) and 5.5% and 1.8% (TSH+T3+T4+AntiTG+Anti-Tpo) in 2008 and 2013, respectively. The increase of the number of requests for serum TSH only, the most appropriate initial thyroid function test, from 6.0% to 30.8% was observed, as well as the switch of T4 and FT4 requests ratio (1.3 vs. 0.2) in favor to FT4 which reflects much better patient's metabolic status than T4. Significant reduction of the number of requests for T3 (91.2% vs. 10.2%) resulted in saving 6.6% of total laboratory annual budget enabling us to introduce new tests e.g. Insulin, C-peptide, ACTH, Thyroglobulin and Anti-CCP.

CONCLUSION

The initiative "from laboratory to clinics" is possible and effective way to implement evidence-based medicine and rational diagnostics in daily laboratory practice. The active laboratory-physician communication ensures using of high quality, cost-effective, logical-sequence protocol for assessment of thyroid function status maintaining the ultimate patient's benefit.