Cardiovascular diseases, including cardiac markers

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USEFULNESS OF NEUROSPECIFIC ENOLASE LEVELS FOR PREDICTING NEUROLOGICAL DAMAGE AFTER RECOVERED CARDIAC ARREST.

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BACKGROUND-AIM

Cardiac arrest (CA) is a major cause of mortality, with neurological damage being the main cause of death in late stages. Serum neurospecific enolase (NE) concentrations are positively correlated with the extent of anoxic-ischemic neurological damage and are a good predictor of unfavorable neurological outcome. The aim of this study was to compare the predictive role of isolated or serial serum NE levels for unfavorable neurological outcome at Intensive Care Unit (ICU) discharge.

METHODS

Prospective study conducted between 2019-2020 in a tertiary hospital. Recovered CA patients admitted to the ICU and a therapeutic controlled normothermia at 37 C were included. NE levels were measured 72-hours after admission [Cobas e411 (Roche,Germany)]. A comparison was made with serial serum levels of a retrospective cohort from 2013 to 2015, of patients undergoing 33 C hypothermia for 24 hours. Epidemiological and clinical variables, laboratory data and Cerebral Performance Category (CPC) score results at ICU discharge were analyzed as an assessment of neurological outcome, comparing the CPC(1-2) group as favorable and CPC(3-5) unfavorable, in the two therapeutic schemes. A Mann-Whitney U was performed and correlated by Spearman's Rho and estimated the predictive power of NE for outcome by Odds ratio (OR). A statistical significance of 5% was considered.

RESULTS

21 patients with a median age of 63 years (p5-p95: 40-77) were included in the normothermia scheme and 29 patients in hypothermia with age 60 years (37-72). A positive correlation was found between NE at 72-hours and CPC (r=0.546;p=0.013) and (r=0.770;p<0.0001) in normothermia and hypothermia respectively. In both therapeutic schemes, NE at 72-hours >25 ng/mL was the best predictor for unfavorable CPC, with OR=18 (95%CI:2-159;p=0.0093) [specificity of 90% for normothermia and 94% in hypothermia (p=0.88)]. In serial determinations, an increase of more than 50 ng/mL between the onset of normothermia and 72-hours had a specificity of 100% for unfavorable CPC at discharge (p=0.013).

CONCLUSIONS

Serial measurements of NE could have a better specificity profile than single values, NE levels >25 ng/mL at 72-hours or >50 ng/mL increase over admission values, are indicative of an increased risk of unfavorable neurologic CPC outcome at ICU discharge.

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HIGHLY SENSITIVE TROPONIN ASSAY AS A SINGLE SERUM TEST IN PATIENTS PRESENTING TO A RAPID ACCESS CHEST PAIN CLINIC IN NON-TEACHING HOSPITAL IN THE UK:

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BACKGROUND-AIM

Evaluation of suspected stable angina patients with probable coronary artery disease(CAD) in the community can be challenging. In the UK rapid access chest pain clinics(RACPC) ensure that these patients are assessed by a specialist within the hospital system. The role of a highly sensitive troponin I(uscTnI) assay in the diagnosis of suspected CAD in a RACPC in a 'real-life' setting in a non-academic hospital has not been explored

METHODS

We investigated the diagnostic value of a uscTnI,(detection limit 0.12 ng/L, upper reference limit 8.15 ng/L and detected uscTnI in 96.8% of the reference population) in a RACPC.

RESULTS

172 RACPC (age 23-88 yr) patients were assigned to either functional or anatomical testing according to the hospital protocol.The proportion of patients, with recorded cardiovascular risk factors were:hypertension (51%), tobacco users (44%), dyslipidemia (48%), diabetes (27%), family history of coronary artery disease (CAD (68%); increased BMI (29%). Calculated QRISK3 ranged from 1-88%, mean 16%. uscTnI ranged from 0.97-9.7 ng/L(normal exercise test,ETT);2.46-17.0 ng/L(abnormal echo);1.8-9.2 ng/L(angina, medication changed);1-70 ng/L(review by specialist);1.5-33.2 ng/L(previous cardiac disease); 0.98-3.9 ng/L(normal stress echo) ;0.58-9.3 ng/L(computerized tomography coronary angiogram(CCTA),normal);1.1-8.7 ng/L(CCTA,CAD positive); 1.1-2.2 ng/L(coronary angiogram negative for CAD); 0.94-49 ng/L(coronary angiogram positive for CAD).Receiver operator characteristic curves with uscTnI values measured in patients who underwent functional testing, angiogram or CCTA, values >0.5 ng/mL showed 100% sensitivity and >11.6 ng/mL showed 100% specificity. In the range 0.5-11.6 ng/mL, uscTnI may not have the same diagnostic potential. In patients assigned to coronary angiogram higher concentrations of uscTnI was associated with severe CAD. Low levels of uscTnI and low pretest probability of CAD(QRISK3) may decrease the number of patients assigned to CCTA.

CONCLUSIONS

The study suggests that uscTnI provides diagnostic value in patients risk-assessed and allocated to CCTA or coronary angiography. ROC curves suggest that diagnostic cut-off values will depend on patient population and their presenting co-morbidity.

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COVID-19 AND CARDIAC BIOMARKERS: WHAT INFORMATION CAN BE DERIVED?

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BACKGROUND-AIM

Covid-19 related severe acute respiratory syndrome can be moderate or severe. In addition to the number of deaths it causes, the after-effects for the survivors on heart, lungs and kidneys are sometimes very severe. We aimed to observe if there exists a relationship between cardiac markers and the risk of death in patients hospitalized with Covid and if concentrations of cardiac markers could be related to the development of post-COVID cardiac, pulmonary or renal conditions.

METHODS

We collected demographic and medical data such as diabetes, cardiovascular, pulmonary or renal conditions for 38 patients (mean age: 64.8±11.9yo) of whom 95% were hospitalized in intensive care unit (ICU), 21 were alive (mean age: 64.5±6.9yo) and 17 died (65.2±16.4yo). All medical records were reviewed for the development of post-Covid cardiac, pulmonary or renal conditions. The following biomarkers were measured: highly sensitive troponin I (hsTnI), creatine-kinase (CK), creatine kinase MB (CKMB) and suppression of tumorogenicity 2 (ST2). We checked the correlation between these and the different conditions.

RESULTS

Among the survivors, 65% developed pulmonary fibrosis, 17% cardiac damage and 22% renal failure. 100% of deceased patients had at least one ST2 value >35ng/mL and 95% for living patients. 53% of living and 77% of deceased patients had at least one hsTnI value >15.6 (women) and >34.2ng/mL (men). 72 % and 17% of living patients had at least one CK value >175UI/L and CK-MB respectively and 50% (CK) and 14% (CKMB) for the deceased patients. We observed that concentrations were higher (mean (and max)) in deceased subjects than in living ones for ST2 (147±57 (180±33) vs 125±64 (156±55) ng/mL), for TnI (902±3172 (2508±5674) vs 397±2104 (1375±37) ng/L), and CKMB (2.4±3.6 (4.3±6.9) vs 1.6±2.3 (3.8±6.4) µg/L) except for CK (203±247 (382±430) vs 1003±3028 (2560±8530) IU/L). No relationship was observed between pulmonary fibrosis and the different markers studied except with troponin (p=0.012). For cardiac and renal damage, no correlation could be demonstrated.

CONCLUSIONS

ST2 and hsTnI were higher in deceased patients, so they may have a predictive value for the risk of death. As most of these patients were on ICU, they were all in a severe condition, making it difficult to differentiate between the deceased and the survivors.

Cardiovascular diseases, including cardiac markers

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BNP AND NT-PROBNP CONCORDANCE FOR RULING OUT HEART FAILURE

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BACKGROUND-AIM

The natriuretic peptides B-type natriuretic peptide (BNP) and NT-proBNP have long standing use in the diagnosis and monitoring of heart failure (HF). Several factors, including increased use of Angiotensin Receptor-Neprilysin Inhibitors e.g. Entresto®, which increases BNP but not NTproBNP and increased accessibility of NP testing to primary care, prompted our laboratory to introduce NT-proBNP in place of BNP. Although BNP and NT-proBNP have shown comparable diagnostic and prognostic performance, discordance of up to 28% has been reported in the acute setting. As part of implementing NT-proBNP, we were interested in studying the concordance between BNP and NT-proBNP.

METHODS

BNP and NT-proBNP were both analysed prospectively on plasma samples (EDTA, n=1048) received for routine patient management between September 2020 and January 2021. Abbott Architect immunoassay I2000SR and Abbott Alinity ci-series analysers were used for BNP and NT-proBNP analysis respectively. Post-analysis, paired BNP and NT-proBNP results were categorised into four groups by patient age (<75y/>75y) and location (acute/non-acute). Acute category was comprised of in-hospital patients including ED and wards. Non-acute included patients from clinics and primary care. Concordance was evaluated using published decision thresholds (ESC, NICE) for ruling out HF in acute and non-acute settings, involving BNP (acute: <100, non-acute: <35ng/L) and NT-proBNP (acute: <300, non-acute <125ng/L). For NT-proBNP, a higher rule out threshold (450ng/L) was applied to patients >75y irrespective of location.

RESULTS

Of the 1048 samples, most were from patients <75y (acute: 42%, non-acute:31%), less than one third from patients >75y (acute: 12%, non-acute: 15%).Concordance was highest (91%) within the <75y non-acute group and least so (85%) within the <75y acute group. Discordant data was largely explained by patients with NT-proBNP above and BNP below respective rule out thresholds.

CONCLUSIONS

In conclusion our large study highlights discordance between BNP and NTproBNP, which is seldom reported, and was informative to the laboratory and clinicians during our implementation of NT-proBNP. Such discordance was largely explained by raised NT-proBNP which could only be explained in part for patients with reduced renal function.

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SIGNIFICANCE OF DETERMINATION OF BCL-2 AND CASPASE-3 ACTIVITY IN ISCHEMIC HEART DISEASE PATIENTS

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BACKGROUND-AIM

Apoptotic cell death may play a critical role in a variety of cardiovascular diseases, especially in those developing on the basis of atherosclerosis. The goal of this study was to compare the activity of caspase-3 and values of Bcl-2 protein in sera in patients with various forms of ischemic heart disease, and to correlate these markers with inflammatory and lipid parameters.

METHODS

We studied 30 patients with chronic stable angina pectoris (SAP), 27 with unstable angina pectoris (USAP), 39 with acute ST-elevation myocardial infarction (STEMI) and 27 age-matched healthy volunteers (Control group). Caspase-3 activity was determined by a colorimetric commercially available method while serum Bcl-2 concentrations were determined using commercially available immunoassays (ELISA).

RESULTS

Caspase-3 was significantly higher only in the USAP group (0.122±0.062 μmol/mg protein, $p<0.05$) in comparison with the control group (0.092±0.022 μmol/mg protein). Concentrations of Bcl-2 were significantly higher in patients with SAP (0.310±0.075ng/mL) and USAP (0.329±0.102ng/mL) compared to healthy (0.250±0.069ng/mL, $p<0.01$) and the STEMI (0.266±0.041ng/mL, $p<0.01$) groups. ROC curve analysis showed that Bcl-2 had the best characteristics in patients with SAP and USAP and represents the best indicator of atherosclerotic plaque activity. However, Bcl-2 could not be a marker of patients' stratification because there was no significant difference between areas of Bcl-2 curves of these two patient groups. These results suggest that simultaneous determination of caspase-3 activity and Bcl-2 can indicate plaque evolution from stable to unstable one.

CONCLUSIONS

The studied markers of apoptosis present valuable parameters in evaluation of atherosclerotic plaque acivity and a new targets for drug therapy.

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SIX-YEAR STORAGE AND MULTIPLE FREEZE-THAW CYCLES DO NOT AFFECT CARDIAC TROPONIN T CONCENTRATIONS MEASURED WITH A HIGH SENSITIVITY CTNT TEST

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BACKGROUND-AIM

High-sensitive cardiac troponin T (hsTnT) is a cardiovascular biomarker making the transition from diagnostic to prognostic use. Determination of long-term stability of hsTnT in frozen clinical specimens is crucial for enabling the intended use of hsTnT as a prognostic biomarker. Therefore, we investigated the effect of long-term storage on hsTnT concentrations.

METHODS

This analysis was part of a larger study investigating the impact of various preanalytical storage conditions on hsTnT concentrations at relevant clinical decision points in venous blood samples from patients admitted to the catherization laboratory for suspected minor myocardial damage. Medical ethical approval was obtained, and all subjects gave written informed consent. For comparison of collection tube, both serum tubes and lithium heparin plasma tubes were drawn from the same patient. Blood was either fresh frozen (centrifuged and frozen immediately) or stored for 3h or 6h at room temperature and then centrifuged/frozen. Afterwards, all samples were stored at -80°C. Samples were thawed for analysis and refrozen at three timepoints (directly after completion of the study (=0 years), after 3-year at -80°C and 6-year at -80°C), resulting in three freeze-thaw cycles. hsTnT concentrations were measured using the fifth generation Roche Diagnostics assay. Statistical analysis was performed using Wilcoxon signed ranks test (test for paired data, for -80°C storage time) or Kruskal-Wallis test (for comparison of preanalytical conditions).

RESULTS

28 patients (164 samples) were included in this analysis. Overall median value of hsTnT concentration was 12.3 ng/L (interquartile range 6.5-24.8 ng/L). hsTnT concentrations after 3-year storage time were not different than at 0-year (P=0.146). The same accounted for 6-year to 0-year (P=0.195). Time before processing or collection tube type did not affect hsTnT (P=1.00 for 0-year storage, P=1.00 for 3-year and P=0.998 for 6-year).

CONCLUSIONS

This study showed that 3-year and 6-year storage at -80°C and up to three freeze-thaw cycles do not affect hsTnT concentrations. Also, time before processing or collection tube type did not affect hsTnT concentration significantly. Our future aim is to determine the effect of 12-year storage on the same samples as well.

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COMPARISON OF LABORATORY AND CLINICAL PARAMETERS AND PSYCHOLOGICAL FUNCTIONING IN CARDIAC PATIENTS DURING THE COVID-19 PANDEMIC

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BACKGROUND-AIM

Depression and anxiety in HF (heart failure) patients are a common occurrence and are associated with a poor clinical picture and prognosis, which may worsen significantly during the COVID-19 pandemic, when patients are exposed to more stress.

METHODS

This study compared hospitalized HF patients' and cardiovascular outpatients' psychological, clinical and laboratory parameters. During two months of the pandemic, hospitalized HF patients completed questionnaires to assess their psychological condition. The cardiovascular outpatient control group completed the questionnaires during their cardiological examination.

RESULTS

The study included 74 hospitalized HF patients (27.03% F and 72.97% M), aged 39 to 89 years (M=70.10 + 11.73) and 74 cardiac outpatients (51.4% F and 48.6% M) aged 27 to 80 years (M=57.35 + 12.61). HF patients were older than outpatients ($t(140)=6.49$, $p<.01$). They had significantly lower left ventricular ejection fraction (35.8 vs. 57.15%; $t(97)=9.08$, $p<.001$), higher heart rate (97 vs. 77/min; $t(101)=5.39$, $p<.001$), and systolic pressure (142 vs. 133 mmHg; $t(102)=2.21$, $p<.05$) in comparison with outpatients. They also had significantly lower cholesterol levels (4.0 vs. 5.9 mmol/L; $t(41)=3.57$, $p<.01$) and LDL cholesterol concentrations (2.4 vs. 3.5 mmol/L; $t(43)=2.80$, $p<.01$).
HF patients had higher level of depression ($r=.38$, $p<.01$), higher fear about heart sensations ($r=.28$, $p<.01$), greater avoidance of activities ($r=.45$, $p<.001$), and more heart-focused attention ($r=.29$, $p<.01$). They reported receiving less support from the environment ($r=-.20$, $p<.05$) but more from health professionals ($r=.30$, $p<.01$).
More depressive HF patients had higher glucose concentration than non-depressive patients. HF patients had elevated NT-proBNP (7297.58 + 8990.11 ng/L) and hs-cTnT (84.52 + 176.46 ng/L) concentrations.
There was a significant correlation between anxiety and NT-proBNP concentrations in hospitalized HF patients ($r=.33$; $p<.05$).

CONCLUSIONS

NT-proBNP is a well-established biomarker for HF. An association was established between elevated NT-proBNP levels and general anxiety symptoms.
This study was funded by the University of Rijeka Multidisciplinary COVID-19 Project.

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DEGRADATION OF NATRIURETIC PEPTIDES BY SACUBITRILAT-INSENSITIVE NEPRILYSIN 2 SUGGESTS DIMINISHED EFFECTS OF SACUBITRILAT BASED HEART FAILURE THERAPY

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BACKGROUND-AIM

Entresto™ is a heart failure (HF) drug combining inhibitors of angiotensin type 2 receptor (valsartan) and neprilysin (NEP) (sacubitril). HF is accompanied by increased production and release by cardiomyocytes of natriuretic peptides (NPs) into the blood in response to ventricular wall distension. By cleaving the active forms of NPs (ANP and BNP) NEP contributes to the reduction of their compensatory effects, whereas inhibition of NEP is believed to potentiate their beneficial effects. A close homologue of NEP, neprilysin 2 (NEP2), has been found in humans; both enzymes share 55% sequence identity and demonstrate a certain degree of similarity in substrate specificity, suggesting a potential contribution of NEP2 to the degradation of NPs. The present study aimed to analyze degradation of NPs by NEP and NEP2 and compare their sensitivity to sacubitrilat.

METHODS

Synthetic human ANP and BNP and recombinant proforms (proANP and proBNP) were incubated with recombinant soluble forms of NEP and NEP2 for different time periods at 37°C in the presence or absence of sacubitrilat. The efficiency of NPs cleavage in the samples was evaluated utilizing in-house sandwich-type immunoassays. The site-specificity of the BNP cleavage was evaluated by immunoassays, based on antibodies specific to neo5 and neo17-epitopes (novel proteolytic epitopes comprising N-terminal Val5 and C-terminal Arg17) and mAb 50E1 (epitope 26-32) as well as by mass-spectrometry.

RESULTS

Both ANP and BNP were susceptible to cleavage by NEP2 in the presence of specific inhibitor of NEP sacubitrilat. NEP2 was able to cleave ANP and BNP at the same sites as NEP. In contrast to NEP, NEP2 was able to cleave proBNP with formation of alternative form BNP 5-32. ProANP was resistant to degradation by both NEP and NEP2.

CONCLUSIONS

The present findings show that sacubitrilat-insensitive NEP2 can contribute to the degradation of ANP and BNP/proBNP diminishing their compensatory effects. These data may shed some light on the exact mechanisms underlying the therapeutic benefit of NEP inhibition in HF and should be taken into consideration while interpreting the results of NPs measurement and choosing therapy.

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LONG TERM EFFECT OF DIFFERENT EDIBLE OILS ON SERUM LIPID PROFILE AND ATHEROGENIC INDICES IN ALBINO WISTAR RATS

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BACKGROUND-AIM

Different types of dietary lipids affect serum lipid profile and lipid metabolism. Vegetable oils are known for their cholesterol-lowering effects when substituted for dietary animal fat; however, specific types of vegetable oils differ in their cholesterol-lowering capacity. In predicting Cardiovascular disease (CVD) risk, especially when absolute values of lipid parameters are not markedly deranged, atherogenic indices contribute significantly. Since changes in the lipid profile have a role in cardiovascular events, in this study we decided to evaluate the long-term effect of commonly used forms of dietary oils (rice bran, sesame, sunflower, coconut, mustard, and cow ghee) on serum lipid profile in Wistar rats.

METHODS

Forty-two female rats were divided into seven groups of six animals each. Groups 1 to 7 received distilled water (DW), rice bran oil (RB), cow ghee (CG), sesame oil (SO), mustard oil (MB), sunflower oil (SUN), and coconut oil (CO) respectively for 120 days (5ml/kg/day, oral). At baseline, and the end of the experiment, fasting blood was collected under anesthesia by retro-orbital puncture method for lipid profile estimation. Data were analyzed using paired t-test and Wilcoxon signed-rank tests based on normality distribution. P-value <0.05 was considered significant.

RESULTS

All the studied oils except cow ghee significantly ($p<0.05$) decreased the total cholesterol (TC) levels post 120 days of oil administration compared to their baseline levels. SO, MO, SUN, and CO significantly ($p<0.05$) decreased the low-density lipoprotein levels compared to its baseline. RB, SO and CO increased the high-density lipoprotein levels, but this increase was statistically not significant. CG significantly ($p<0.05$) increased the atherogenic index of plasma (AIP). RB, SO, MO, SUN, and CO significantly ($p<0.05$) decreased the cardiac risk ratio (CRR) and atherogenic coefficient (AC).

CONCLUSIONS

In this study, we have observed that except for CG all oils reduce the TC levels. RB, SO, MO, SUN, and CO significantly decreased the atherogenic indices (CRR, AC), which indicates the beneficial effects of these dietary oils. Although few findings of this study are in line with previous reports, none of them studied the long-term effect (120 days) of vegetable oils.

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ASSOCIATION BETWEEN SERUM IONIZED MAGNESIUM AND PROGRESSION OF AORTIC VALVE CALCIFICATION

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BACKGROUND-AIM

Several recent clinical studies have demonstrated that hypomagnesemia is associated with vascular calcification. However, to date, little is known about the association between serum magnesium (Mg) level and aortic valve calcification.

METHODS

In an ongoing prospective cohort of aortic stenosis (AS) patients (n= 356), serum Mg was measured at baseline both in its ionized (iMg) and total (tMg) forms. AS severity was evaluated at baseline and yearly thereafter using mean pressure gradient (MPG), Peak velocity (VMAX), aortic valve area indexed to body surface (iAVA) assessed by transthoracic echocardiography and the degree of aortic valve calcification (AVC) assessed by computed tomography. Annual progression (n = 290) was calculated as: final measurement-baseline measurement)/follow-up duration. Associations were evaluated using the student T-test and multivariate logistic regression.

RESULTS

At baseline, lower iMg and tMg were significantly associated with sex, diabetes, tobacco use and hypertension but not with AVC neither with MPG nor iAVA. There was a highly significant correlation between iMg and tMg concentrations. Almost 37% and 25% of patients had low iMg values (normal range 0.45-0.60 mmol/L) and low tMg values (normal range 0.80-0.95 mmol/L), respectively. After mean follow-up of 2.5 ± 2 years, the annual mean Log AVC progression was significantly greater (p = 0.01) in patients with iMg values ≤ 0.45 mmol/L (2,04 ± 0.73) as compared to patients with iMg > 0,45 mmol/L (1.78 ± 0.94). Mean MPG and iAVA also progressed more in patients with low iMg but without reaching significance. In multivariate analysis, iMg remained associated with the progression of AVC independently of several cofactors, including baseline AVC.

CONCLUSIONS

In a prospective cohort of asymptomatic patients with a wide range of AS severity, our study demonstrated that low serum ionized Mg but not low total Mg was independently associated with AVC progression

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CLINICAL USE OF AMINO-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE IN PLEURAL FLUID

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BACKGROUND-AIM

The amino-terminal fragment of prohormone of brain natriuretic peptide (NT-pro-BNP) measured in serum has an established role in the diagnosis, management and prognosis of patients with congestive heart failure. The purpose of our study was to evaluate and compare different cut-off points for NT-pro-BNP values measured in pleural fluid and serum in patients with pleural effusion due to different etiologies and to establish an appropriate cut-off value for pleural effusions of cardiac origin.

METHODS

We collected pleural fluid samples sent in a lithium heparin tube over a three-year period. Samples were analyzed with the Cobas e602 and e411 analyzer (Roche Diagnostics) by electrochemiluminescence immunoassay. The cut-off value for BNP was determined by the receiver-operating characteristic curve.

RESULTS

53 samples of pleural fluid were analyzed. The etiology of pleural effusion in 32 (60.4%) of the samples was congestive heart failure. The remaining 21 (39.6%) samples presented a different origin: infectious or malignant. Of the 32 samples with cardiac origin, 23 (71.9%) were from men with a median age of 74 years and 9 (28.1%) were from women with a median age of 78 years. On the other hand, of the 21 samples with different origin, 13 (21.9%) were from men with a median age of 71 years and 8 (38.1%) were from women with a median age of 61 years. The average pleural fluid of NT-pro-BNP levels for cardiac origin were 7131.2 pg/mL and 5488.6 pg/mL for non-cardiac origin. As to NT-pro-BNP in serum the average levels for cardiac origin were 7923.1 pg/mL and 1414.3 pg/mL for non-cardiac origin.
The area under the curve was 0.73 for the pleural NT-pro-BNP and 0.810 for the serum determination. The optimal cut-off point for the pleural fluid was 853 pg/mL with a sensitivity of 93.75% and specificity of 52.38% and 1478 pg/mL for serum levels with a sensitivity of 84.38% and specificity of 78.57%.
For a sensitivity of 97% the cut-off value was 514 pg/mL for both determinations with a negative predictive value of 91% in pleural fluid and 83% in serum.

CONCLUSIONS

Our study suggests that NT-pro-BNP can be useful in clinical practice to exclude cardiac etiology of pleural effusions. The diagnostic accuracy of the pleural measurement is affected by the lack of specificity of pro-BNP in patients with multiple pathologies. This could represent a confounding factor that potentially decreases the specificity of NT-proBNP levels for the diagnosis of cardiac pleural effusion and explain our higher cut-off points than those described in other studies.

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EARLY RULE OUT OF MYOCARDIAL INFARCTION FOR A WHOLE BLOOD HIGH SENSITIVITY CARDIAC TROPONIN I POINT OF CARE ASSAY COMPARED TO A CENTRAL LABORATORY ASSAY

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BACKGROUND-AIM

High sensitivity (hs) cardiac troponin (cTn) assays are defined per the IFCC Committee on Clinical Applications of Cardiac Biomarkers (C-CB) by the ability to measure > 50% of concentrations greater than the limit of detection (LoD) with an imprecision of <10% at sex-specific 99th percentiles. hs-cTn assays have been utilized as part of early rule out strategies for myocardial infarction (MI) based on a single specimen collection at presentation in emergency department (ED). Our study determined the clinical performance of a single measurement to rule out acute MI in patients presenting to the emergency department (ED) in whom serial cTnI measurements were obtained on clinical indication.

METHODS

This was a prospective, observational study of consecutive patients presenting to the ED (n=1089) in whom hs-cTnI measurements were obtained (clinicaltrials.gov NCT04772157) by the Siemens Atellica® VTLi WB POC hs-cTnI assay and the Abbott ARCHITECT i2000 plasma hs-cTnI assay. We determined negative predictive values (NPV) and sensitivities (SENS) for ruling out MI at concentrations that were optimized for NPV at >99.5%.

RESULTS

Acute MI occurred in 91 patients (8.3%), including 23 (25%) type 1 MI and 68 (75%) type 2 MI. For the POC VTLi hs-cTnI and Abbott ARCHITECT plasma hs-cTnI assays respectively, 21% (n=230) and 26% (n=287) of patients were identified for rule out using baseline samples only. Optimized NPVs for ruling out were: WB POC at < 4 ng/L – 99.6% (90% CI: 98.8-100.3); plasma central lab at < 4ng/L 99.6% (90% CI 99.0-100.2). Sensitivities at these respective NPVs were: WB POC 98.9% (90% CI 97.1-100.6); plasma central lab 98.7% (90% CI 97.1-100.6).

CONCLUSIONS

Our findings show the novel, whole blood POC Atellica® VTLi hs-cTnI assay provides a unique rule-out strategy using a single hs-cTnI measurement at presentation alone, to assist in early rule and discharge of low-risk patients presenting to an inner-city ED. The POC hs-cTnI assay observations were comparable to an established central laboratory hs-cTnI assay that used plasma. The use of an early rule out strategy allows the immediate identification of patients in whom the clinical presentation is unlikely to be due to either type 1 or type 2 MI. The implementation of this approach may reduce overcrowding, facilitate early discharge in selected patients, expedite triaging and reduce costs, predicated on a POC hs-cTnI assay. (Information presented in this paper is based on research results that are not commercially available in any country. The VTLi assay is not available for sale in the USA.)

Cardiovascular diseases, including cardiac markers

M164

THE CAPACITY OF APOB-DEPLETED PLASMA IN INDUCING ATP-BINDING CASSETTE A1/G1-MEDIATED MACROPHAGE CHOLESTEROL EFFLUX—BUT NOT GUT MICROBIAL-DERIVED METABOLITES—IS INDEPENDENTLY ASSOCIATED WITH MORTALITY IN PATIENTS WITH ST-SEGMENT ELEVATION MYOCARDIAL I

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BACKGROUND-AIM

Impaired HDL-mediated macrophage cholesterol efflux and higher circulating concentrations of trimethylamine N-oxide (TMAO) levels are independent risk factors for cardiovascular mortality. The TMAO precursors, γ-butyrobetaine (γBB) and Trimethyllysine (TML), have also been recently associated with cardiovascular death, but their interactions with HDL-mediated cholesterol efflux remain unclear.

METHODS

We aimed to determine the associations between APOB depleted plasma-mediated macrophage cholesterol efflux and plasma TMAO, γBB, and TML concentrations and explore their association with two-year follow-up mortality in patients with acute ST-elevation myocardial infarction (STEMI) and unstable angina (UA).

RESULTS

Baseline and ATP-binding cassette transporter ABCA1 and ABCG1 (ABCA1/G1)-mediated macrophage cholesterol efflux to APOB-depleted plasma was decreased in patients with STEMI, and the latter was further impaired in those who died during follow-up. Moreover, the circulating concentrations of TMAO, γBB, and TML were higher in the deceased STEMI patients when compared with the STEMI survivors or UA patients. However, after statistical adjustment, only ABCA1/G1-mediated macrophage cholesterol efflux remained significantly associated with mortality. Furthermore, neither the TMAO, γBB, nor TML levels altered the HDL-mediated macrophage cholesterol efflux in vitro.

CONCLUSIONS

Our results demonstrate that impaired ABCA1/G1-mediated macrophage cholesterol efflux is independently associated with mortality at follow-up in STEMI patients. These results motivate further research on therapeutic strategies aiming to improve the ABCA1/G1-mediated macrophage cholesterol efflux capacity in this group of patients.

Cardiovascular diseases, including cardiac markers

M165

RELATIONSHIP OF THE THIGH CIRCUMFERENCE AND ZINC-α2-GLYCOPROTEIN (ZAG) IN THE GENERAL POPULATION

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BACKGROUND-AIM

A low thigh circumference is associated with cardiovascular (CV) diseases and total mortality, however the exact underlying pathophysiological mechanism remain unclear. The aim of the study was to examine the association of thigh circumference and biochemical parameters.

METHODS

931 individuals aged 20-79 were analyzed in the Bialystok Plus study (Poland). Data were collected through standardized health examinations center. The measurement of thigh circumference were performed directly below the gluteal fold. Zinc alfa2-glcoprotein (ZAG) and adiponectin were measured manually by ELISA method from R&D systems. Cortisol and total testorene (TT) were determined by the electrochemiluminescence method on the Cobas e411 from ROCHE. The free testosterone (FT) was calculated (CFT) by published methods by Ly and Handelsman. Association between thigh circumference and biochemical variables were analysed using simple and multiple linear regression models. Multiple linear models were adjusted for age, sex (Model 1), for age, sex, body mass index (BMI) (Model 2), and for age, sex, BMI, cortisol, (Model 3). Statistical hypotheses were verified at a 0.05 significance level. The IBM SPSS Statistics 20.0 statistical software (Armonk, NY, USA) was used for all calculations.

RESULTS

The mean age of study population was 49.1±15.5 years and 56.8% female. The mean thigh circumference was 58.2±5.9 cm. In linear regression models, a higher thigh circumference were associated with lower level of cortisol (B -0.145, p<0.001), ZAG (B -0.276, p=0.039) and adiponectin (B -0.188, p=0.003). In models adjusted by BMI only ZAG was significantly correlated with thigh circumference (Model 2: B -0.188, p=0.021; Model 3: B -0.227, p=0.013). Cortisol, CFT and adiponectin were not independently related to the thigh circumference.

CONCLUSIONS

The association between thigh size and biochemical parameters is mediated by BMI, and a parameter independent of BMI that could affect the circumference of the thigh is ZAG. Higher thigh circumference is associated with lower ZAG levels.

Cardiovascular diseases, including cardiac markers

M166

HIGH-SENSITIVE CARDIAC TROPONIN VALUES IN WOMEN WITH SUSPECTED ACUTE MYOCARDIAL INFARCTION: THE IMPORTANCE OF P99.

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BACKGROUND-AIM

Ultrasensitive troponin I is a highly useful biomarker in the diagnosis of acute myocardial infarction (AMI). Since February 2021, the measurement of high-sensitive troponin I (HS-cTnI) has been implemented in our laboratory, which allows to measure lower cTnI values and delta variations.
According to our protocol, in patients with suspected AMI with a first HS-cTnI value greater than the 99th percentile (p99), a second measurement should be made after 3 hours, and the delta variation should be studied. Currently, in order to simplify the new protocol, p99 has been established at 11ng/L, regardless of patient's sex. p99 in women is recommended to be 9ng/L, so 11ng/L could decrease sensitivity in women with suspected AMI.
Women which are suffering AMI present more varied and atypical symptoms. It can delay the diagnosis and increase mortality, so it's essential to rule it out correctly when there are suggestive symptoms.
The aim of this descriptive retrospective study is to review the diagnosis in women, with HS-TnI value between 9 and 11ng/L, in order to analyze if there is a decrease in sensitivity in the diagnosis of AMI.

METHODS

After 5 months working with the new protocol, we reviewed the HS-TnI results obtained in women at emergency department, with suspected AMI and a baseline troponin value between 9-11ng/L. The reason for consulting and definitive diagnosis was collected too.

RESULTS

During this time, 3,792 troponin determinations were made in 2,579 patients (1,046 women). Of these, 37 belongs to women with an initial value between 9-11ng/L, with a mean age of 69.8. In 35.14% of the cases, a second determination was requested after 3 hours in order to study delta variation.
The main reasons for consultation were: dyspnea (21.62%), chest pain (24.32%) and dizziness or syncope (16.21%). No patient was diagnosed with AMI, but 7 patients were diagnosed with other cardiac pathology, and 3 already had it previously.

CONCLUSIONS

With the data presented, there is not a decrease in sensitivity regarding the diagnosis of AMI for women when p99 is 11ng/L instead of 9ng/L. However, it's a very small number of patients, it is necessary to collect more data in order to continue with the study and draw new conclusions.

Cardiovascular diseases, including cardiac markers

M167

CARDIAC TROPONIN AND MYOCARDIAL DAMAGE INDEX

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BACKGROUND-AIM

Postoperative cardiac troponin I (Tn) elevation is a common phenomenon with several potential mechanisms that often leads to diagnostic confusion. The aims of this study were to determine the dynamics of Tn levels after cardiac surgery and to develop a method for assessing myocardial damage and the risk of complications in the postoperative period.

METHODS

Patients undergoing cardiac surgery (109 men, mean age 54.3 ± 7.5 years), were randomized into 3 groups: (1) coronary artery bypass grafting (CABG) and novel technique of preconditioning induction (n=29), (2) conventional CABG (n=60), (3) aortic valve replacement (n=20). The operations were performed using cardiopulmonary bypass and isothermal blood cardioplegia. Tn levels were measured before operation and 2,6,12,24,48 hours after the surgery using immunochemical analyzer (Architect i2000SR, Abbott Diagnostics).

RESULTS

Concentration of Tn increases in all patients 2 hours after surgery, and it increases more than tenfold in the 99th percentile, which is caused by damage to cardiomyocytes during surgical manipulations on the heart. None of the patients experienced perioperative myocardial infarction (type 5). The maximum release of Tn in group (1) was 1819±178 ng/L after to 2 h, in group (2) - 1632±224 ng/L after to 24 h, in group (3) - 2923±377 ng/L after to 6 h surgery. Two patterns of Tn release were noted in the postoperative period with peak concentrations at 2-6 h or 12-24 h after surgery. In patients with peak Tn concentration occurring at 12-24 h there was a tendency towards a longer hospitalization time and higher blood lactate levels (4,1±0,7 mmol/l; p=0.001). Therefore, it is proposed to measure the levels of Tn after surgery twice, after 2-6 hours (early Tn) and after 12-24 hours (late Tn), then calculate the myocardial damage index (MDI) as the ratio of late Tn to early Tn. ROC analysis showed that the if MDI was 1.8 or more, myocardial damage and the risk of postoperative complications should be considered high.

CONCLUSIONS

Peak Tn at 2-6 h following cardiac surgery appears to be related to the surgical process and non-specific myocardial injury whilst a continuing increase at 12-24 h indicates an increase in the damage zone. We would suggest Tn sampling at 2-6 and 12-24 h post cardia# surgery and calculating the MDI for the routine detection of the size of myocardial damage.

Cardiovascular diseases, including cardiac markers

M168

DEVICE-MEASURED MOVEMENT BEHAVIORS AND CARDIAC MARKERS IN OLDER ADULTS

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BACKGROUND-AIM

Cardiac troponin T-high sensitive (cTnT-hs) and N-terminal pro-brain natriuretic peptide (NT-proBNP) are essential markers for the diagnosis of myocardial infarction and heart failure, respectively. As both markers, as well as less physical activity (PA) and more sedentary time, are related to higher cardiovascular risk, we aimed to investigate the association between device-measured movement behaviors and these cardiac markers in older adults.

METHODS

We used data from 1939 individuals aged ≥65y without cardiovascular disease (CVD) participating in the Seniors-ENRICA-2 study. Wrist-worn ActiGraphGT9X accelerometers during 7 days were used to assess time in movement behaviors: sedentary behavior (SB) defined as <45mg, light PA (LPA) as 45-99mg, moderate-to-vigorous PA (MVPA) as ≥100mg. Cardiac markers were measured on Cobas®6000 (Roche). Analyses using linear regression models adjusted for the main confounders were conducted separately in 4 groups based on subclinical cardiac damage and total PA time. Subclinical cardiac damage was defined as cTnT-hs >p99 (men: 16.8pg/dL, women: 9.0pg/mL) or NT-proBNP >75 or >250pg/mL if aged 50-75 or >75y, respectively. Total PA time was stratified by the study median (3.44h/d).

RESULTS

In the less active individuals with subclinical cardiac damage, 30 min/d more of SB, LPA and MVPA were associated with mean percentage differences (95% confidence interval) in cTnT-hs of 2.6% (1.5,3.8), -4.5% (-7.1,-1.9) and -14.2% (-18.0,-10.2), respectively; corresponding values for NT-proBNP were 2.2% (0.3,4.1), -11.0% (-14.9,-6.8) and -14.7% (-21.0,-7.9). However, in the more active participants with subclinical cardiac damage, cTnT-hs was a 3.6% (1.2,6.0) higher for each 30min/d more of LPA, and no associations were seen for SB or MVPA. No associations were apparent in participants without subclinical cardiac damage save a 8.6% (0.7,15.9) lower NT-proBNP for each 30min/d more of MVPA in those less active.

CONCLUSIONS

The relationship between movement behaviors and cardiac markers in older adults without CVD depends on subclinical cardiac damage and PA level. The strongest associations were observed in less active individuals with subclinical cardiac damage, in whom more PA and less SB were related to lower cTnT-hs and NT-proBNP levels.

Cardiovascular diseases, including cardiac markers

M169

EXTRACELLULAR VESICLES IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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BACKGROUND-AIM

Circulating extracellular vesicles is involved in pathogenesis of cardio-vascular diseases including chronic thromboembolic pulmonary hypertension (CTEPH). They are important regulators of endothelial function, inflammation and coagulation, and levels can fluctuate with disease severity in patients with CTEPH.
Aim of the study is to analyze an amount of vesicles shed by different cells type.

METHODS

19 patients of Almazov National Medical Research Centre CTEPH Registry (median age=50.5 [39.5; 64]; 7 male, 12 female) and 10 healthy donors (median age=48 [40.1; 53.8]; 5 male, 5 female) were included in the study. CTEPH diagnosis was verified according to European Society of Cardiology guidelines 2009, 2015. All participants gave informed written consent. Experiments were approved by the Local Ethics Committee according to Declaration of Helsinki. Blood samples were collected in vacuum tubes with K2EDTA as anticoagulant. The samples were tested for complete blood count, C-reactive protein (CRP) and D-dimer levels. Exosomes isolation was carried out using Exo-FACS kit (HansaBioMed Life Sciences, Estonia) according to the manufacturer's protocol. Fluorescently labeled exosomes: CD41 (platelets), CD45 (leukocytes), CD235a (erythrocytes) and CD105 (endotheliocytes) were analyzed using flow cytometry (CytoFlex B4-R2-V2, Beckman Coulter, USA).

RESULTS

Levels of CD41+ exosomes were higher in CTEPH patients compare to donors (40.75% [29.7; 55.8] vs 27.2% [22.55; 31], p=0.013); levels of CD105+ exosomes showed a 2.5-fold increase (4.8% [3.25; 10.35] vs 1.9% [1.43; 2.8], p=0.003). Levels of CD45+ (8.3% [3.75; 9.55] vs 8.8% [7.48; 10.88]) and CD235a+ (5.2% [4.3; 6.4] vs 6.15% [5.28; 6.88]) exosomes were not differ (p=0.278 and p=0.156). We obtained significant positive correlations between CD41+ exosomes and CRP (r=0.786, p=0.021) and D-dimer levels (r=0.510, p=0.044) in CTEPH patients. Significant positive correlations between CD41+ and CD105+ exosomes (r=0.733, p=0.025); CD45+ exosomes and WBC (r=0.767, p=0.016) and neutrophils count (0.817, p = 0.007) were shown.

CONCLUSIONS

The increase of platelet- and endothelium-derived exosomes levels in CTEPH patients may explain pathophysiological mechanism of haemostasis activation and inflammation.
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Cardiovascular diseases, including cardiac markers

M170

POINT-OF-CARE HIGH-SENSITIVE TROPONIN-I ANALYSIS IN CAPILLARY BLOOD FOR ACUTE CORONARY SYNDROME DIAGNOSTICS

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BACKGROUND-AIM

When a patient enters the emergency department with signs and symptoms of a myocardial infarction, fast and accurate chest pain assessment is needed to distinguish between high risk and low risk patients. This differentiation remains a diagnostic challenge, whereby point-of-care testing can contribute to earlier disposition decisions for patients excluded from Acute Coronary Syndrome (ACS). This study focuses on the analytical and clinical performance of capillary samples as measured on the Atellica® VTLi Patient-side Immunoassay Analyzer device for high-sensitive troponin I.

METHODS

152 patients with acute chest pain admitted to the cardiac emergency department (ED) were included in the study. Capillary blood collected at the cardiac ED was compared with whole-blood and plasma samples obtained by venipuncture. All samples were analyzed using the Atellica® VTLi device; in addition, plasma was analyzed by a central laboratory immunoassay analyzer.

RESULTS

All sample types correlated very well with Pearson's $r \geq 0.995$. No significant difference was observed between venous whole blood versus plasma analyzed by the Atellica® VTLi device. The difference between capillary blood and venous samples showed a constant bias of 7.1%, for which a correction factor has been implemented. The overall analytical agreement between capillary POC results compared to plasma analyzed with a central laboratory immunoassay analyzer was 97.4%. No clinically relevant differences were observed between the two methods.

CONCLUSIONS

The POC Atellica® VTLi Patient-side Immunoassay Analyzer device for high-sensitive troponin I analysis shows equivalent results for all sample types, including capillary blood. No clinically relevant differences were observed between capillary POC and central laboratory results. Looking forward, POC testing could pave the way toward rapid testing of troponin in the ambulance or the general practitioner’s office, which could help to differentiate between high- and low-risk patients.

Cardiovascular diseases, including cardiac markers

M171

CHANGES IN BLOOD IONIZED MAGNESIUM CONCENTRATIONS DURING CARDIAC SURGERY

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BACKGROUND-AIM

Magnesium (Mg) is crucial during cardiac surgery which involves extracorporeal circulation (ECC). Therefore, patients need to be given significant amounts of Mg during surgery, but little is known about the consequent concentrations of Mg in the blood, especially ionized Mg (iMg). Ionized Mg is considered to be the only physiologically active form of Mg and its clinical determination has until recently been limited by unsatisfactory methodology.

METHODS

The concentrations of iMg were anaerobically determined in the arterial blood of 73 patients using the Stat Profile Prime Plus Critical Care blood gas analyzer. Cardiac surgery included either bypass procedures or valve implantations.

RESULTS

The mean value ± standard deviation (m.v. ± SD) of iMg, expressed in mmol/L, were: before heparinization and ECC 0.54 ± 0.07, 5 min after ECC initialization 1.02 ± 0.28, 5 min before ECC termination 0.97 ± 0.18, 1h after surgery 0.77 ± 0.12, following morning 0.66 ± 0.08, second morning 0.61 ± 0.08, third morning 0.59 ± 0.09 and at discharge 0.59 ± 0.07 (usually 6 to 8 days after surgery, venous blood was used).

CONCLUSIONS

Test results showed that patients, at the beginning of the surgery, had iMg values below internal stated reference interval. Mg administration significantly increased iMg levels during surgery. After surgery and during postsurgical hospitalization, iMg levels gradually decreased in a nonlinear way. At discharge, the iMg levels were still within the reference interval. The results suggest that personalized Mg administration during surgery, with close monitoring of iMg, and multi-day Mg supplementation before surgery might be beneficial to sustain optimal iMg levels.

Cardiovascular diseases, including cardiac markers

M172

COMPARATIVE STUDY OF NATRIURETIC PEPTIDES IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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BACKGROUND-AIM

Natriuretic peptides (PN) are hormones that have natriuretic and vasodilator properties. They are synthesized and stored in myocytes, releasing in response to ventricular dysfunction. They are good biomarkers for early diagnosis and risk stratification, especially in heart failure (HF).
The New York Heart Association (NYHA) scale provides a simple classification of the severity of HF, categorizing patients according to their limitation to physical exercise.
Analysis of NPs according to prognosis based on the NYHA classification in the studied cohort.

METHODS

To assess the degree of HF involvement versus physical exercise, the NYHA scale is used, divided into 4 classes: Class I: asymptomatic - without limitation of physical activity (PA), Class II: mild symptoms and slight PA limitation, Class III: marked PA limitation and Class IV: severe limitation.
Plasma is studied in the first 24 hours of 200 patients who after suffering an acute myocardial infarction (AMI) have been admitted to the Coronary Unit between 2018-2019. 30 Blood Bank donor controls are studied. NTproBNP and BNP are determined simultaneously by chemiluminescence immunoassay on ARCHITECT i2000 (ABBOTT).

RESULTS

The results of the natriuretic peptides have been evaluated based on the average number of times that the limit of normality is exceeded for each peptide, in the case of BNP above 100 pg / mL and in the case of NTproBNP above 450 pg / mL in each class and in the control group.
In Class I (N: 149, 68.7%), age: median 60 years, 1.8 times for BNP and 3.4 times for NTproBNP.
In Class II (N: 39, 23.4%), age: median 77 years, 5.2 times for BNP and 15.4 times for NTproBNP.
In Class III (N: 11, 7.4%), age: median 84 years, 7.0 times for BNP and 19.4 times for NTproBNP.
In Class IV (N: 1, 0.5%), age: 55 years, 14.8 times for BNP and 29.8 times for NTproBNP.
In control group (N: 30), age: median 51 years, 0.21 times for BNP and 0.14 times for NTproBNP.

CONCLUSIONS

68.7% of the cases studied did not present limitation of habitual PA after suffering an AMI, but it was observed that older patients present a slight and marked limitation in habitual PA. As the NYHA classification progresses, higher values are observed on average of the number of times normality is exceeded for both NPs (without taking into account class IV due to presenting a single case), from class I to III, from 3.8 to 5.7 times for BNP and NTproBNP respectively, not showing a similar increase for both peptides.

Cardiovascular diseases, including cardiac markers

M173

HIGH SENSITIVITY TROPONIN I TESTING DURING OUT-OF-HOURS IN A TERTIARY CARE HOSPITAL IN SRI LANKA

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BACKGROUND-AIM

High sensitivity troponin I (hs TnI) test was introduced recently for out of hours to Provincial General Hospital, Badulla which is a tertiary care hospital in Sri Lanka. Our aim was to examine the patterns of troponin testing during out of hours and its effect on patient management including length of stay

METHODS

This was a retrospective study in which medical records of all adult patients underwent troponin testing during out of hours at PGH, Badulla during the month of October 2019 were analysed using SPSS 20 version. High sensitivity troponin I was measured in Abbott Architect i1000 SR and sex specific 99th percentiles were used to categorise patients into positive and negative groups.

RESULTS

A total of 250 patients were included in the study. The majority of patients had negative troponin results (68.8%). Out of troponin positive patients 55.1% were treated as ACS, 51.3% patients were referred for cardiology opinion and 65.4% had final diagnoses associated with a cardiac condition such as heart failure, an acute coronary syndrome and arrhythmias. Individuals with positive troponin tests had a significantly longer length of stay (median, IQR (Interquartile range): 5, 5) compared to those with negative tests (median, IQR: 2, 2; $P < 0.05$).

CONCLUSIONS

A positive troponin test was associated with increased length of stay. Only half of patients were referred to the cardiologist and others would not have been considered as having a significant cardiac condition. This may reflect the routine ordering of hs troponin I rather than based on patient's clinical condition. Therefore guidelines need to be provided to ensure that troponin is requested only in cases where an ACS is suspected.

Cardiovascular diseases, including cardiac markers

M174

PROGNOSTIC VALUE OF CARDIAC BIOMARKERS SOLUBLE ST2, TROPONIN I, AND NT-PROBNP IN TYPE 2 DIABETES: A 15-YEAR FOLLOW-UP STUDY

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BACKGROUND-AIM

Patients with type 2 diabetes (T2D) present a substantially increased risk of cardiovascular (CV) disease and mortality. Assessment of circulating biomarkers of cardiac damage and remodeling might represent a feasible approach to improve the prediction of CV outcomes in T2D.

METHODS

Here, we measured serum levels of soluble suppression of tumorigenesis-2 (sST2), high-sensitive cardiac troponin I (hs-cTnI), and N-terminal pro-BNP (NT-proBNP) by fully automated assays in 415 patients with T2D with 15-year follow-up information available on survival and development of T2D complications, and in 127 healthy control subjects (CTR).

RESULTS

Serum sST2 and hs-cTnI were higher in T2D patients compared to CTR, while no significant difference was observed for NT-proBNP. Notably, sST2 levels followed an increasing trend from CTR to uncomplicated T2D patients (T2D-NC) to T2D patients with at least one complication (T2D-C), whereas hs-cTnI was significantly higher in T2D-C compared to CTR but not to T2D-NC. As expected, the levels of the three biomarkers were significantly higher in T2D patients with a history of major adverse cardiovascular events (MACE). In all groups, serum sST2 levels were significantly higher in males compared to females, while NT-proBNP was higher in females. Different from the other biomarkers, sST2 showed a weaker positive correlation with age and its levels were associated with biochemical variables representing glycemic control and liver function. Multiple Cox regressions, adjusted for age, sex, and HbA1c, revealed a significant association between sST2 and 15-year mortality in T2D patients (C-index=0.718), with patients with the highest sST2 levels (≥37.3 ng/mL) having a 5-fold increased risk of death (HR: 5.07, 95% CI: 1.32-19.49) compared to patients with low (<16.5 ng/mL) serum levels. In combination, sST2, hs-cTnI, and NT-proBNP significantly predicted all-cause mortality (C-index=0.736) and the development of MACE.

CONCLUSIONS

In conclusion, the ability of sST2 to predict all-cause mortality and MACE in the long term and its ability to track variables related to insulin resistance and associated metabolic disorders better than conventional cardiac biomarkers support its implementation into the routine clinical practice, especially in the follow-up of patients with T2D.

Cardiovascular diseases, including cardiac markers

M175

QUANTIFICATION OF CARDIAC TROPONIN BY LANTHANIDE-LABELLING AND ELEMENTAL MASS SPECTROMETRY

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BACKGROUND-AIM

Cardiac troponin (cTn) is the gold standard biomarker used for diagnosis of cardiovascular diseases (CVDs). In 2019, 32 % of all global deaths were attributed to CVD, where myocardial injury was considered the major cause. When heart muscle tissue is damaged, cTn is released into the bloodstream. The concentrations found in blood are often in the low µg/L range and below, which makes the detection of cTn challenging. The current state-of-the-art is to measure cTn using high sensitivity ELISAs which have limits of quantification (LOQ) as low as 1 ng/L. However, these tests often show discordant results and, thus, reference measurement procedures are required to provide anchor points for routine methods and to enable truly comparable results.

METHODS

Two different approaches using inductively coupled plasma mass spectrometry (ICP-MS) detection were investigated: An intact protein- and a specific peptides-based approach.
After an initial test using the protein's constituent sulfur to quantify cTn failed, labeling of the cysteines in cTnI with a lanthanide-DOTA complex was applied to enhance sensitivity in the ICP-MS for both the peptides and the whole protein. For the peptide-based approach, the cTnI was enzymatically digested by GluC to yield specific peptides, which were separated on a reversed phase-column which was directly coupled to the ICP-MS. To improve the LOQs, an enrichment step using protein G functionalized magnetic beads with an anti-cTnI antibody to capture and separate the cTn from the matrix was developed. To measure the whole protein, the cTnI bound to the magnetic beads was directly injected into the ICP-MS, leading to an improved sensitivity.

RESULTS

Without enrichment, labelled protein specific synthetic peptides could be detected down to 25 nmol/L peptide in solution, corresponding to 600 µg/L cTn. After enrichment, around 10 µg/L of TnI in buffer could be measured.
First experiments detecting the whole protein show promising results with LOQs in the upper ng/L range. The specificity and potential interferences of this approach are currently being investigated.

CONCLUSIONS

Promising results were achieved for the detection of cTnI in calibration solutions. However, for quantification in serum, the methods require further optimization to reach the required LOQs.