

dicting CVD risk in clinical practice. If important characteristics such as age, sex and history of CVD are available, pragmatic imputation of median values results in reliable predictions.

Funding Acknowledgements: In part by a grant from the American Heart Association Award Number 17IGMV33860009

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Multilocus association analysis identifies genetic predictors of essential hypertension

Y. Timasheva¹, T. Nasibullin¹, A. Zakirova², O. Mustafina¹. ¹Institute of Biochemistry & Genetics, Ufa Science Centre of Russian Academy of Science, Ufa, Russian Federation; ²Bashkir State Medical University, Ufa, Russian Federation

Background and purpose: Candidate-gene and genome-wide association studies have been successful in discovering new genetic loci associated with hypertension and related traits. However, identifying informative genetic predictors of essential hypertension still remains one of the most important challenges of personalized predictive medicine. Chronic low-grade systemic inflammation and endothelial dysfunction are recognized as the major pathogenic processes driving the development of hypertension. We aimed to identify inflammation-related genetic predictors of essential hypertension using multilocus approach.

Methods: We performed comparative analysis of transcriptional activity of inflammatory mediator genes in patients with essential hypertension and healthy normotensive subjects using real-time PCR primer assays (SABiosciences, Qiagen, USA), and genotyped polymorphic markers in 14 differentially expressed chemokine genes (CCL2, CCL8, CCL16, CCL17, CCL18, CXCL1, CXCL8, CXCL13, CCR2, CCR5, CXCR2, CXCR4, CX3CR1, CCL23) in the group of 526 male individuals (212 cases, 314 controls) of Tatar ethnic origin from the Republic of Bashkortostan (Russian Federation). We analyzed associations of chemokine loci with essential hypertension using logistic regression with age and body mass index as covariates under additive genetic model implemented in PLINK software. Multilocus associations were tested with APSampler 3.6.0 using Markov chain Monte-Carlo-based approach. Benjamini-Hochberg procedure was applied to adjust for multiple comparisons.

Results: Analyzing polymorphic loci in 14 chemokine genes, we found that CXCL13 rs355689 polymorphism was independently associated with essential hypertension (OR=0.51, PFDR=9.56x10⁻⁴ for the C allele). Using multilocus approach, we obtained 2587 patterns associated with essential hypertension. The most informative predictors were CCL17*T + CCL8*C + CX3CR1*T + CXCL13*C (OR=0.17, PFDR=4.08x10⁻⁴), CCL2*A + CCL17*T + CCL8*C + CXCL13*C (OR=0.17, PFDR = 2.85x10⁻⁴), CXCR4*T + CCL18*C + CCR2*I (OR=8.13, PFDR=0.009), CXCR4*C + CCL17*C/C + CX3CR1*T (OR=2.64, PFDR=0.007).

Conclusion: Using single-marker approach, we detected an association between CXCL13 rs355689 polymorphism and essential hypertension. Applying APSampler algorithm, we revealed additional associations of the combinations of the studied loci with hypertension. Our results suggest that multilocus approach is more powerful in identifying genetic predictors of the disease.

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Multicentric analysis of adverse cardiovascular events in cocaine abuse patients in india

S. Tanwar¹, N. Sen², A. Jain², R.K. Gokhroo³, A. Mehta⁴. ¹HG SMS Hospital, Preventive Cardiology, Jaipur, India; ²Narayana Hrudayalaya, Cardiology, Jaipur, India; ³J L N Medical College, Cardiology, Ajmer, India; ⁴Kokilaben Dhirubhai Ambani Hospital, Mumbai, India

Background: Cocaine may cause coronary vasoconstriction and endothelial dysfunction. Understanding the relationship between cocaine abuse, a common and theoretically modifiable condition, and the most common cause of death in the world, cardiovascular disease, may inform potential prevention strategies.

Purpose: The study sought to investigate the associations among cocaine abuse and unstable angina (UA), atrial fibrillation (AF), myocardial infarction (MI), and congestive heart failure (CHF).

Methods: We performed a longitudinal analysis of young Indians 18 to 45 years of age who received ambulatory surgery, emergency, or inpatient medical care in India different medical or cardiac centers between 2010 and 2016. We determined the risk of an cocaine abuse diagnosis on incident AF, UA, MI, and CHF. Patient characteristics modifying the associations and population-attributable risks were determined.

Results: Among 11435 patients, 237 (2.07%) had cocaine abuse. After multivariable adjustment, cocaine abuse was associated with an increased risk of incident UA (HR: 1.46; 95% CI: 1.41 to 1.52; p<0.005, MI (HR: 1.43; 95% CI: 1.40 to 1.49; p<0.004), (HR: 1.45; 95% CI: 1.40 to 1.51; p<0.005), AF (hazard ratio [HR]: 2.05; 95% confidence interval [CI]: 2.04 to 2.13; p<0.004), and CHF (HR: 2.27; 95% CI: 2.23 to 2.36; p<0.005). In interaction analyses, individuals without conventional risk factors for cardiovascular disease exhibited a disproportionately enhanced risk of each outcome. The population-attributable risk of cocaine abuse on each outcome was of similar magnitude to other well-recognized modifiable risk factors.

Conclusions: Cocaine abuse increased the risk of UA, AF, MI, and CHF to a similar degree as other well-established risk factors. Those without traditional cardiovascular risk factors are disproportionately prone to these cardiac diseases in

the setting of cocaine abuse. Thus, efforts to mitigate cocaine abuse might result in meaningful reductions of cardiovascular disease.

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A new efficient and flexible cardiovascular risk model for working population

L.M. Ruilope¹, C. Fernandez-Labandera², P. Valdivielso³, M.A. Sanchez-Chaparro³, C. Catalina-Romero², L. Quevedo-Aguado², P. Martinez-Munoz², E. Calvo-Bonacho². ¹University Hospital 12 de Octubre, Hypertension Unit, Madrid, Spain; ²Ibermutuamur, Madrid, Spain; ³University of Malaga, Malaga, Spain. On behalf of IberScore

Background: Identifying people at high cardiovascular risk (CVR) is challenging, especially at young age. The SCORE predictive function has been used for long time in Spain for predicting the absolute risk of suffering a fatal cardiovascular event in 40–65 year-old population.

Purpose: The main objective of the IberScore Study was to derive a mathematical model for risk prediction of fatal and non-fatal cardiovascular events from a relatively young and healthy working population.

Methods: A predictive function for fatal and non-fatal CV events was derived from a cohort of 774,404 workers (70.4% of the target population), free of CV disease at entry, who were followed during 10 years. Workers ages ranged 16–65 years (mean 35.7, SD 10.7). 71.7% were men, which represented the real proportion in the target population.

Results: Along the 10-year follow-up we found 3,762 first cardiovascular events (6‰) in derivation cohort. Most of them (80.3%) were non-fatal ischemic events. We derived a logistic flexible parametric model to predict 10-year cardiovascular risk. 82% of those who suffered a cardiovascular event during the follow-up span had been previously classified as “high risk” or “very high risk” using our model, whereas only 12% of them were classified in the same groups using SCORE. The latter also showed a weak discrimination power for risk stratification while IberScore clearly distinguished the four risk categories.

Conclusions: IberScore worked much better to estimate cardiovascular risk in a relatively young and healthy Spanish working population when compared to other models. Cardiovascular aging, as the result of the effects of risk factors, should be at the core of CV risk estimation. Cut-off points should be set considering the benefit we seek with the treatments we have in mind.

Funding Acknowledgements: Research project grant (FIS PI12/02812) from the Health Institute Carlos III and the Spanish Ministry of Economy and Competitiveness of Spain

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Is exercise capacity above 4METs good enough to screen pre-operative patients with non-cardiac surgery?

S. Taniai, J. Ito, T. Yorozu, H. Yoshino. Kyorin University, Second Department of Internal Medicine, Mitaka, Japan

Background: We developed a new cardiovascular screening system named as “Cardiac Preoperative Screening (CPS)” which is used to evaluate the needs for cardiac consultation for patients who have scheduled non-cardiac surgery.

By modifying the guidelines of ACC/AHA 2007 and ESC/ESA 2014 for Noncardiac Surgery, we created new screening system, CPS. In the guidelines, the exercise capacity above 4METs is the key marker of the acceptance of perioperative evaluation and management for planned noncardiac surgeries. However, whether the exercise capacity above 4METs is safe enough to undergo the non-cardiac surgery remains uncertain.

Purpose: The purpose of this study is whether the exercise capacity above 4METs to screen preoperative patients is sufficient to rule out from possible cardiac events or not.

Methods: This study included a total of 12,841 consecutive patients (5,788 male, age 57±17 y/o) who underwent planned adult non-cardiac surgery. Patients answered the interview sheet 1 month before surgery about the presence of active cardiac conditions, such as, unstable coronary syndrome, decompensated heart failure, symptomatic supraventricular or ventricular tachycardia, and severe valvular heart disease; exercise capacity above 4METs; and clinical risk factors, such as, history of acute coronary syndrome, history of heart failure, history of stroke, diabetes mellitus or chronic kidney disease. Patients were classified into 4 categories; C1 to C4; C1 (their exercise activity is above 4METs without cardiac symptom), C2 (less than 4METs with no clinical risk factors), C3 (less than 4METs and at least 1 clinical risk factor) and C4 (with unstable symptoms). In CPS, the patients in C1 were classified into “Active group”, and patients in C2 and C3 were classified into “Inactive group” according to the exercise capacity of above 4METs or less, respectively.

Results: Of 12,841 cases, CPS was performed in 11,161 cases (86.9%). Active group: 10,081, Inactive group: 787 cases. Among 10,868 cases, total cardiac events developed in 135 cases (1.24%), including 22 coronary ischemic events (0.20%). The event-rate of total cardiac events was higher in Inactive group than in Active group (2.5% vs. 1.1%, P=0.002), and of coronary ischemic events (1.02% vs. 0.14%, P<0.001). In Active group, preoperative drug intervention of concerning events was treatments of statin (OR 1.83; 95% CI 1.12–2.97, p=0.016) and calcium channel blocker (OR 1.69; 95% CI 1.11–2.58, p=0.015), but in inactive group, there was no relationship between drug intervention and events.