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Freie Vorträge - Biomarker bei ACS

V1616 - A new method to adjust Troponin I accounting for the confounders age, gender and kidney function facilitates clinical interpretation in patients with chest pain

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Background and Objectives: Cardiac Troponin (cTn) is the gold standard biomarker for diagnosis of acute myocardial infarction (AMI). Several variables such as gender, age and kidney dysfunction are known to affect troponin levels. This results in the recommendation of different diagnostic cut-offs for troponins in specific settings e.g. females or elderly. Unfortunately, application of multiple cut-offs at the same time is rather impractical in clinical routine. We aimed to develop a method to adjust for multiple confounders prior to clinical application. Thereby, keeping the unified established 99th percentile diagnostic cTn cut-off. Further, this approach will be validated in a real world cohort of patients with suspected AMI.
Methods and Results: To develop our adjustment model we used a cohort of 4587 individuals of the prospective longitudinal *Diabetes Cardiovascular Risk Evaluation Targets and Essential Data for Commitment of Treatment* (DETECT) study representing unselected consecutive individuals presenting to a general practitioner irrespective of symptoms or diagnoses. Here, cTnI showed the expected correlation with age and estimated glomerular filtration rate in males and females with r_{age}=0.436/0.518, p<0.001/<0.001 and with r_{eGFR}=-0.142/-0.207, p<0.001/<0.001. For the adjustment we took these variables as covariates in a linear regression model with cTnI as dependent variable, and then moved each patient?s cTnI value along the regression line to the empirical mean as evaluation point, in each dimension. In a second step, this adjustment model was applied in a real world cohort of 1789 (m/f, 1193/596) patients with suspected AMI (407 with final diagnosis AMI). As outcome measure we used the area under the curve (AUC) in the receiver operator characteristic analysis as well as specificity of our adjusted cTnI compared to the unadjusted cTnI using the unified 99th percentile cut-off for identification of AMI. For convenient use, a smartphone app was developed.
Adjusted cTnI compared to unadjusted cTnI yielded comparable AUCs to identify AMI with 0.952 (0.938-0.965) and 0.957 (0.944-0.970) in males as well as 0.940 (0.909-0.970) and 0.945 (0.917-0.973) in females excluding a relevant loss of diagnostic information due to the adjustment.
The specificity for AMI in patients older than 70 years was improved by the adjusted cTnI with 0.96 (0.92-0.98) in males and 0.93 (0.88-0.97) in females compared to 0.84 (0.79-0.89) and 0.87 (0.80-0.91) if using unadjusted cTnI values. Analogously, the specificity was improved in patients with renal dysfunction to 0.95 (0.89-0.98) in males and 0.86 (0.78-0.92) in females using adjusted cTnI values compared to 0.83 (0.74-0.90) and 0.77 (0.68-0.85) associated with raw cTnI values.
Conclusion: Adjustment of cTnI values with respect to confounding factors substantially improves the diagnostic ability of cTnI to rule-in AMI in e.g. elderly patients or patients with impaired renal function. Interpretation of cTnI values in complex emergency cases is therefore facilitated especially by maintaining the single established diagnostic 99th percentile cut-off in all patients.

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