Modification of GRACE score with genetic markers in patients with acute coronary syndromes

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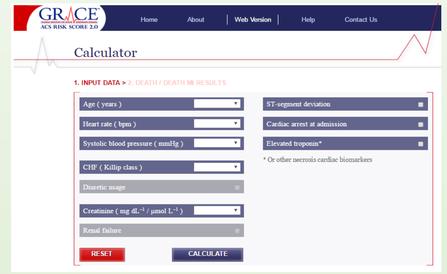
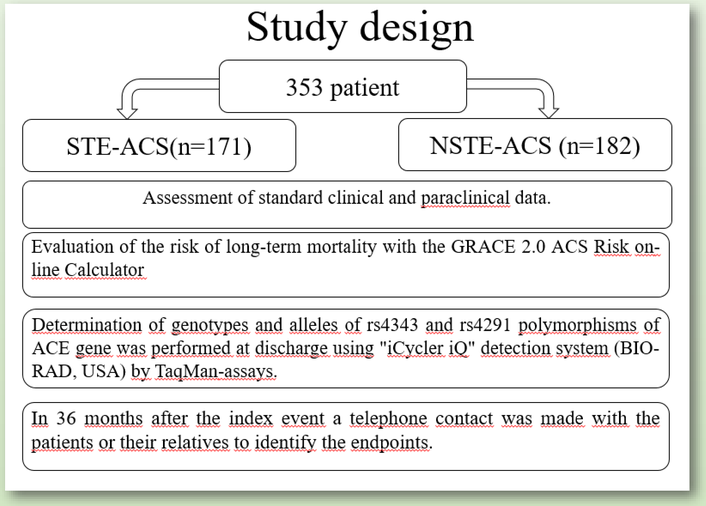
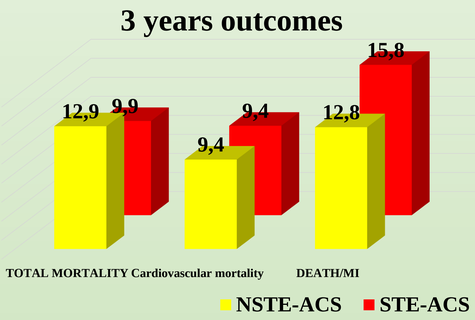


Purpose. We aimed to assess the possibility to improve a predictive capability of GRACE 2.0 risk score using additional accounting of the genotypes of rs4291 and rs4343 polymorphisms of ACE gene in patients with ST-segment elevation acute coronary syndrome (STEMI) and non-ST-segment elevation acute coronary syndrome (NSTEMI).

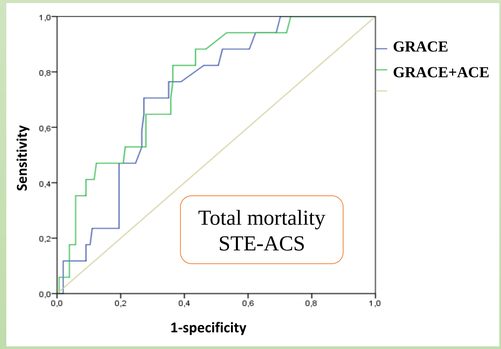


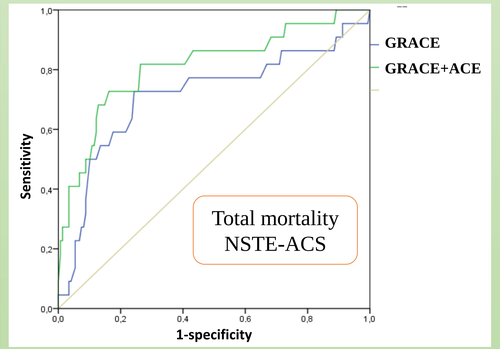


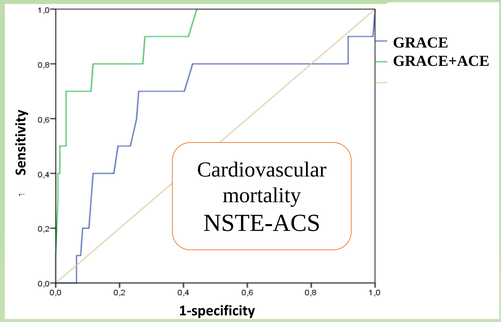
Material and methods. The prospective study included 171 patients with STEMI and 182 patients with NSTEMI admitted to a cardiology dispensary within 48 hours since the onset of symptoms. A risk score of long-term mortality was calculated using GRACE 2.0 ACS Risk on-line Calculator (http://gracescore.org/WebSite/ WebVersion.aspx). Determination of genotypes and alleles of rs4343 and rs4291 polymorphisms of ACE gene was performed at discharge using "iCycler iQ" detection system (BIO-RAD, USA) by TaqMan-assays. Additional exclusion criteria were clinically significant comorbidities. In 36 months after the index event a telephone contact was made with the patients or their relatives to identify the endpoints. We succeeded to specify a patient's status "dead or alive" in 96.6 % of cases. In NSTE-ACS and STE-ACS a mortality from any causes was 12.9% (n=22) and 9.9% (n=17) correspondingly, cardiovascular mortality – 9.4% (n=16) and 9.4% (n=16) and the incidence of endpoints "cardiovascular death/nonfatal myocardial infarction" – 12.8% (n=21) and 15.8% (n=27).

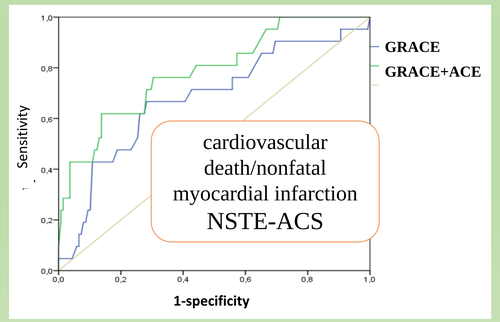
Results. A combination of TT genotype of rs4291 polymorphism and GG genotype of rs4343 polymorphism of ACE gene was conclusively associated with three-year total mortality both in STEMI ($p = 0.02$) and in NSTEMI ($p < 0,0001$). However, a statistically significant relationship of these genotypes with cardiovascular mortality as well as the risk of death/nonfatal MI was revealed only in NSTEMI. The ROC-curves analysis showed that in NSTEMI a combined use of GRACE score with rs4291 and rs4343 polymorphisms had significantly ($p < 0.0001$) increased its predictive capability in regard to all previously described endpoints. Thus, the values of the area under ROC-curves in prognosis of total mortality were 0.71 (0.58-0.85) and 0.81 (0.70-0.92) for GRACE and GRACE+ACE scores correspondingly, in prognosis of cardiovascular mortality – 0.66 (0.46-0.87) and 0.91 (0.82-0.99) and in prognosis of cardiovascular mortality/nonfatal MI – 0.68 (0.55-0.81) and 0.79 (0.68-0.89). As concerns the STE-ACS a significant ($p = 0.001$) improvement of prognostic value of GRACE score supplemented by the identification of rs4291 and rs4343 polymorphisms was obtained only for total mortality within three years. Thus, the values of the area under ROC-curves for GRACE score and the own model (GRACE+ACE) were 0.72 (0.62-0.82) and 0.77 (0.66-0.87 correspondingly.

ROC curves of GRACE and GRACE + ACE models









<u>Conclusion. Modification of GRACE 2.0 score by adding the data on the genotypes of rs4291 and rs4343 polymorphisms of ACE gene more effectively improves the mortality prediction within three years after NSTEMI than after STEMI.</u>