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Prognostic value of admission glycaemic excursions in elderly patients with acute coronary syndrome

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Background and aims: Acute phase hyperglycaemia has been associated with increased mortality in patients with acute coronary syndrome (ACS). However, the predictive value of admission glycemic excursions for adverse outcome in elderly ACS patients is unknown. This study is to investigate the prognostic value of admission glycemic variability for one-year major adverse cardiac event (MACE) in elderly patients with ACS.
Materials and methods: 186 elderly ACS patients' clinical data were collected and the GRACE risk score were calculated as admission. The fluctuations of glucose levels in patients were measured by a continuous glucose monitoring system (CGMS) for 72 hours. The occurrence of MACE in patients was documented during one year follow-up. All participants were grouped into tertiles of mean amplitude of glycemic excursions (MAGE), absolute means of daily differences (MODD) and postprandial glucose excursion (PPGE) to compare the baseline data, the level of GRACE risk score and the incidence of MACE among the subgroups. A multivariate Logistic stepwise regression model was made to explore the independent contribution to cardiovascular outcomes.
Results: In all patients, a higher MAGE, MODD or PPGE level was associated with advanced age, the higher levels of heart rats, admission blood glucose and hemoglobin A_{1c}, the lower level of left ventricular ejective fraction value, and a higher GRACE risk score and higher incidence of MACE. The same results were also found in elderly ACS patients with and without diabetes history. Levels of MAGE (4.07±1.37 mmol/L vs. 2.77±1.37 mmol/L, p<0.001), MODD (2.66±1.01mmol/L vs. 1.62±0.76mmol/L, p<0.001) and PPGE (6.06±2.61 mmol/L vs. 3.47±2.13 mmol/L, p<0.001) were significantly higher in patients with MACE than in patients without MACE. Multivariate analysis indicated that age, previous CAD history, high-sensitive C reactive protein, admission blood glucose, eGFR, MAGE and MODD were independent determinants for MACE. After adjusting for GRACE risk score, diabetes history, hypoglycemic therapy and other confounders, MAGE (p=0.003) and MODD (p=0.052) levels retained a significant independent association with occurrence of MACE.
Conclusion: The admission intraday and interday glycemic variability may be associated with the outcome of elderly patients with ACS. Acute glycemic excursions, as one of components of the dysglycaemia, should not be neglected in ACS patients.
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Glycaemic variability and ventricular cardiac arrhythmias in type 2 diabetic patients with chronic heart failure

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Background and aims: Prevalence of chronic heart failure in population with diabetes is wide. Ventricular arrhythmias seem one of the factors that determine the prognosis of heart failure. It has to be checked whether glycaemic variability has an influence on ventricular cardiac arrhythmias in type 2 diabetic patients with chronic heart failure.
Materials and methods: An observational study was performed. 80 type 2 diabetic patients with chronic heart failure were included. The severity of heart failure was estimated by a 6-minute walk test and by the echocardiography, 48 patients (60%) characterized by III and IV functional class of heart failure. The median of duration of diabetes was 11 years. 40 patients (50%) used oral hypoglycaemic agents, 36 (44%) - insulin as monotherapy or in combination with oral medication, 5 (6%) - on the diet. Follow-up was 6 months. The study protocol included a 3-fold daily Holter electrocardiogram monitoring: at the inclusion visit, at 3 months and 6 months. Patients kept diaries of self-control blood glucose levels and hypoglycaemic events. During the day of Holter monitoring glucose was studied before meals, 2 hours after main meals, at bedtime and 3 am. Combined simultaneous monitoring (Holter + continuous glucose monitoring) was performed in 20 patients. We used the CGM system by Medtronic MiniMed (USA) and the "Myocard-Holter" (NIMP ESN Ltd, Russia). Ventricular arrhythmias 4-5 and E-D gradations by Myerburg R.J. (2001) were regarded as dangerous. The parameters of glycaemic variability were also examined.
Results: 7 patients died during the study. Dangerous ventricular arrhythmias were detected in 42 patients (51 %) in 3-fold Holter monitoring. Glucose less than 5 mmol / l during the day of Holter increased 4.8 times the risk of dangerous arrhythmias (p = 0.03; logistic regression). Mean Amplitude of Glycaemic Excursion (MAGE) was associated with dangerous ventricular arrhythmias. There is a direct correlation between the level of MAGE and the number of ventricular premature beats (r = 0.54; p = 0.02, Spearman). MAGE in patients with arrhythmias was 5.3 mmol/l [4.9; 6.3], in cases without arrhythmias - 2.4 mmol/l [2.0; 3.0] (p=0.006, Mann _ Whitney U-test). Prevalence of dangerous ventricular arrhythmias in cases with MAGE > 5 mmol/l was 43 %, in cases with MAGE < 5 mmol/l - only 8 % (p=0.02, Pearson Chi-square).
Conclusion: The high glycaemic variability (MAGE > 5.0 mmol / l) is associated with dangerous ventricular arrhythmias. The high glycaemic variability is a proarrhythmic factor in type 2 diabetic patients with heart failure.

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Glycaemic fluctuations and arrhythmias in type 2 diabetes with cardiovascular disease

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Background and aims: Patients with type 2 diabetes and cardiovascular disease (CVD) may represent a high risk group for arrhythmias and sudden death in hypoglycemic episodes. Little is known on frequency of asymptomatic hypoglycemia and its relationship to arrhythmias. By parallel measurement of interstitial glucose (i. G.) concentrations with continuous glucose measurement system (CGMS) and long-term ECG recording (LT-ECG) we therefore analysed the following questions in a high risk cohort:
1 - Relationship between low i. G. concentration and frequency of arrhythmias
2 - Relationship between fluctuation and frequency of arrhythmias
3 - Critical arrhythmias and their determinants
Materials and methods: 23 patients with type 2 diabetes, HbA1c <9 %, age 50 - 80 years, with proven CVD, treated with insulin and/ or sulfonylurea were considered. CGMS with Medtronic MiniMed Gold ™ system and ECG with Amedtec ECG pro • were recorded in parallel for 5 days and we analysed the frequency of ventricular extrasystoles and salvos, supraventricular extrasystoles and measured cQT-time. Hypoglycemia by CGMS was defined as modest (3.1-3.9 mmol/L) or severe (<3.1 mmol/L). The patients noticed symptoms of hypoglycemia and arrhythmias in a predefined protocol.
Results: The patients recorded only few mild symptomatic hypoglycemia. However we observed a high frequency of silent hypoglycemic episodes by CGMS. No arrhythmias were reported by the patients although we observed serious ventricular arrhythmias like ventricular tachycardias by LT-ECG. Hypoglycemic episodes and arrhythmias were most frequent at night.
Conclusion: Patients with CVD on insulin or sulfonylurea treatment represent a high risk for silent hypoglycemia and arrhythmias. Avoidance of excessive glucose fluctuations in glucose lowering treatment might be of importance to protect patients with CVD from arrhythmias.

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A short-term improvement of blood glucose control increases aspirin sensitivity in aspirin-resistant type 2 diabetic men

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Background and aims: Aspirin is recommended to the majority of patients affected by type 2 diabetes mellitus (T2DM) although the aspirin-induced prevention of cardiovascular events is smaller in diabetes than in the general population. Determinants of the aspirin resistance and of its reversibility in T2DM, however, are poorly clarified. We aimed at verifying whether in T2D

men a short-term improvement of blood glucose (BG) control influences aspirin resistance.

Materials and methods: T2DM men with HbA1c >7.5% (n=37, age: 61.6±1.2 years, known diabetes duration 12.8±1.1 years, BMI: 29.6±0.60 kg/m², HbA1c: 8.9±0.14%), on 100 mg/day aspirin were submitted to a 3-month intervention aiming to reach the best possible BG control by implementation of hypoglycaemic therapy with a careful avoidance of hypoglycemia. No change in hypolipidemic or anti-hypertensive treatment was allowed. Before and after the intervention, platelet sensitivity to aspirin was evaluated by Platelet Function Analyzer-100 (PFA-100): the cut-off for aspirin sensitivity is a closure time >200 sec. Among many other parameters, we evaluated: blood pressure (BP), hemoglobin A1c (HbA1c), fasting and post-prandial BG, lipids, von Willebrand Factor (vWF), a determinant of PFA-100 response. Data are expressed as mean±SEM. To compare subjects within and between the two groups, two factor mix design ANOVA and Spearman' correlation analysis were used.

Results: At baseline, aspirin sensitive (n=27, 73%) and aspirin resistant (n=10, 27%) subjects did not significantly differ for age, known diabetes duration, BMI, systolic and diastolic BP, HbA1c, fasting and post-lunch BG, HDL-cholesterol, triglycerides, and vWF, whereas aspirin-resistant subjects presented higher levels of total cholesterol (185.3±8.9 vs 156.6±5.4 mg/dl, p<0.009), LDL-cholesterol (105.3±14.3 vs 70.6±8.7 mg/dl vs, p<0.05) and apo B100 (93.0±4.9 vs 77.2±3.0 mg/dl, p=0.009). BG variables decreased after the intervention in aspirin sensitive and in aspirin resistant patients: i) HbA1c, from 8.8%±0.2% to 7.6%±0.1% (p<0.0001) and from 9.2%±0.3% to 7.6±0.2% (p<0.0001), respectively; ii) fasting BG, from 177.8±7.2 to 153.4±5.6 mg/dl (p<0.002) and from 181.7±11.9 to 134.3±9.1 mg/dl (p<0.0001), respectively; ii) post-lunch BG, from 182.1±9.3 to 144.4±6.9 mg/dl (p<0.0001) and from 186.3±15.3 to 148.0±11.3 mg/dl (p<0.009), respectively. PFA-100 values did not change in patients already aspirin-sensitive at baseline, but significantly improved in the aspirin-resistant-ones, from 149.2±10.4 to 228.5±15.0 sec (p=0.0001). In aspirin-resistant subjects baseline values of PFA negatively correlated with HbA1c (rho=-0.835, p=0.003) and fasting BG (r=-0.806, p=0.05).

Conclusion: i) 27% of poorly controlled T2DM men are aspirin resistant; ii) aspirin resistant T2DM men are characterized by higher values of total and LDL-cholesterol and of apoB-100 vs the aspirin sensitive-ones; iii) in aspirin resistant T2DM men, platelet sensitivity to aspirin strongly correlates with the BG control, whose improvement is accompanied by a decrease of aspirin resistance. Thus, BG improvement plays a major role in the reversal of aspirin insensitivity in T2DM men.

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Short- and long-term survival in Scottish cancer patients with and without co-morbid type 2 diabetes (1997-2007)

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Background and aims: Cancer patients who have pre-existing diabetes at diagnosis are at greater risk of long-term all-cause mortality than those without diabetes. However, relatively few studies have examined how the influence of diabetes on survival varies for specific cancers throughout the time period after cancer is diagnosed. This study investigated short- and long-term survival in Scottish cancer patients with and without Type 2 diabetes (T2DM) for cancer of the breast, lung, prostate and colon/rectum.

Materials and methods: Data from a population-based national diabetes register and the Scottish Cancer Registry were used to investigate associations between co-morbid diabetes (at the time of cancer diagnosis) and all-cause survival in the intervals 0 to 1 year, >1 to 2 years, >2 to 5 years and over five years after diagnosis. People in Scotland diagnosed with any of the cancers of interest during 1997 to 2007 were followed up until the end of 2010. Cox regression models incorporating terms representing the interaction between time and presence of T2DM were fitted to estimate the hazard ratio (HR; T2DM vs. no diabetes) in each interval. Separate models were fitted for each combination of sex and cancer site. Estimates were adjusted for age at cancer diagnosis, socio-economic status (SES) and cancer stage at diagnosis (breast and colon/rectum only). All models were re-fitted with additional predictors representing broad categories of cancer treatment (surgery, radiotherapy, chemotherapy). Cumulative incidence functions were calculated and plotted to provide insight into the respective probabilities of death from the index cancer and from any other cause over the period studied.

Results: Numbers of patients without diabetes ranged from a minimum of 12,082 (female; cancer of the colon/rectum); the corresponding number with pre-existing T2DM was 948. During the intervals 0 to 1 year and >1 to 2 years post diagnosis, survival did not differ significantly by diabetes status for any cancer. In the interval >2 to 5 years, survival in the T2DM group was poorer in men with prostate cancer (HR 1.28; 95% confidence interval [CI] 1.15 to 1.41) and, marginally, in women with colorectal cancer (HR 1.18; 95% CI 1.01 to 1.38). Over the interval >5 years, significantly elevated risk in the T2DM group was observed for all sex/site combinations except women with lung cancer. Hazard ratios for men in this interval were lowest for prostate cancer (HR 1.33; 95% CI 1.16 to 1.52). For women, the least elevation of risk was for lung cancer (HR 1.31; 95% CI 0.84 to 2.03). Further adjustment for cancer treatment did not materially change the results. Examination of cumulative incidence functions indicates that the respective probabilities of death from the index cancer and from any other cause differ markedly across cancer sites.

Conclusion: This study indicates that the presence of co-morbid Type 2 diabetes at the point of cancer detection does not influence survival (in respect of death from any cause) during the first two years after cancer is diagnosed. Over a more extended period, the influence of co-morbid T2DM varies by sex and cancer site, with higher risk generally observed in those with diabetes over the interval beyond 5 years. This elevation of risk may reflect less aggressive cancer therapy received by patients with co-morbid diabetes, and the increased susceptibility of people with diabetes to death from causes other than cancer (e.g. heart disease).

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High proinsulin levels are independently associated with 20-year cancer mortality. The Hoorn study

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Aims: High proinsulin levels are associated with all-cause and cardiovascular mortality. It is unclear whether they are associated with cancer mortality