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CDE Academy - Diabetes Literature Review

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Painless myocardial infarction: at very high risk

An interesting study on painless ST-elevation myocardial infarction (STEMI) was presented by a multidisciplinary team comprising emergency doctors from Singapore General Hospital and physicians from the epidemiology and public health department and the National Heart Centre in this island city-state of 5.4 million people.

The aim of this retrospective study using data from the national myocardial infarction registry was to improve outcomes in patients with silent myocardial infarction. The study measured door to balloon (D2B) time and the effect of treatments in patients from this registry who presented with painless myocardial infarction at emergency room arrival. 30-day mortality and side effects of treatments were studied.

From January 2010 to December 2012, 6,412 cases of STEMI were collected, of which 1,745 patients were not included in the study. In total, 10.9% of selected patients presented with painless STEMI.

Clinical signs at presentation in patients without chest pain included difficulty breathing (56.6%), syncope (6.7%) and sweating (diaphoresis) (19.8%). The mean age of patients with painless STEMI was higher than that of the other STEMI patients (75 versus 58 years). There were also more women (39.9% versus 16.11%) and more patients with hypertension (71.1% versus 54.6%).

This study also confirmed the classical notion that diabetes is significantly associated with an absence of chest pain (48.6% of painless STEMI patients had diabetes versus 37% without diabetes). The same was true of patients with a prior myocardial infarction (20% versus 12.3%).

For patients with painless STEMI, not only was D2B time longer (80 versus 63 minutes, $p<0.01$), but 30-day mortality was markedly higher (34% versus 4.8%).

In conclusion, silent myocardial infarction, which accounts for about 10% of cases, is associated with a very high risk as well as a delay in initiation of reperfusion therapy. It is therefore imperative to increase the rapidity of diagnosis and the effectiveness of treatments in order to improve the prognosis in these patients.

Pin Pin Pek et al. (2015). Reperfusion treatment delays amongst patients with painless ST-segment elevation myocardial infarction. *19th World Congress on Disaster and Emergency Medicine – WADEM,* Cape Town, 21 – 24 April 2015

Should butter intake be reduced to a minimum with hypercholesterolaemia?

Butter is especially rich in saturated fats, particularly palmitic and myristic acids which are known for their hypercholesterolaemic effects. This is the main reason behind the recommendation to limit butter intake in people with cardiovascular risk factors. Several clinical trials have shown that high butter intake on a daily basis increases LDL cholesterol, but generally does not affect HDL cholesterol levels. On the other hand, the effect of moderate butter intake had not been rigorously examined until the study by Sara Engel and Tine Tholstrup sponsored by the Danish Dairy Research Foundation.

Butter or olive oil

This double-blinded crossover dietary intervention study was conducted in 47 volunteers (33 women and 14 men, mean age 40 years, mean body mass index (BMI) 23.5 kg/m², mean LDL cholesterol 2.88 mmol/L). The subjects' habitual dietary pattern was modified during two 5-week periods ('butter intake' and 'olive oil intake'). During the 'butter' period, subjects ate buttered bread (approximately 15 g of butter, the exact amount being calculated so that 4.5% of total energy came from butter). During the 'olive oil' period, subjects ate bread spread with olive oil (containing an identical amount of fats). Each period was preceded by a 14-day run-in during which subjects consumed their habitual dietary patterns. Subjects were weighed each week and the investigator checked that there was no change in the level of physical activity or dietary habits outside of what was prescribed.

A marked effect of butter on LDL cholesterol

Compared with the 'olive oil' period, the 'butter' period increased LDL cholesterol by 5.6% (from a mean of 2.88 mmol/L to 3.04 mmol/L). While butter intake also led to an increase in HDL cholesterol, olive oil had no effect on this parameter. Neither butter nor olive oil had any effect on plasma triglycerides, homeostatic model assessment (HOMA)-estimated insulin resistance, or high sensitivity c-reactive protein (CRP), a marker of infraclinical inflammation.

"there is a larger than expected effect of butter on LDL cholesterol levels and pointed out that the potential cardiovascular consequences are significant because a 1 mmol/L decrease in LDL cholesterol over the long term is associated with a 20% reduction in cardiovascular mortality."

The authors noted a larger than expected effect of butter on LDL cholesterol levels. They pointed out that the potential cardiovascular consequences are significant because a 1 mmol/L decrease in LDL cholesterol over the long term is associated with a 20% reduction in cardiovascular mortality. Furthermore, while observational epidemiological data indicate that raising HDL cholesterol could theoretically counteract the increase in LDL cholesterol, this hypothesis has been widely questioned by recent data showing that increasing HDL cholesterol is not systematically beneficial. In fact, it is probably the quality of HDL particles, i.e. their antiatherogenic function, rather than their quantity in plasma that should be improved in order to lower cardiovascular risk, and the effect of butter on this function of HDL cholesterol is not known.

This study therefore shows that moderate daily intake of butter for several weeks has a cholesterol-raising effect. This confirms the recommendation that consumption of butter should be kept to a minimum in people with hypercholesterolemia and/or at high cardiovascular risk.

Engel S et al.: Butter increased total and LDL cholesterol compared with olive oil but resulted in higher HDL cholesterol compared with a habitual diet. ***Am J Clin Nutr.*** **2015; 102:309-15.**

Type 1 diabetes as a risk factor for heart failure

Background

Diabetes is an established risk factor for heart failure, but because nearly all heart failure occurs in older individuals, the excess risk and risk factors for heart failure in individuals with type 1 diabetes are not known.

We aimed to determine the excess risk of heart failure in individuals with type 1 diabetes overall, and by different levels of glycaemic control and albuminuria.

Methods

In this prospective case-control study, we identified:

- all individuals with type 1 diabetes registered in the Swedish National Diabetes Registry between January 1, 1998, and December 31, 2011, and
- five controls randomly selected from the general population for each person, matched according to age, sex, and county.

We compared them with respect to subsequent hospital admissions for heart failure, with hazard ratios calculated with Cox regression.

"Individuals with type 1 diabetes had a four-times increase in the risk of being admitted to hospital with heart failure compared with population-based controls."

Findings

In a cohort of 33 402 individuals (mean age at baseline 35 years [SD 14], 15 058 [45%] women, and mean duration of diabetes 20·1 years [SD 14·5]), over a mean follow-up of 7·9 years, 1062 (3%) individuals were admitted to hospital with a diagnosis of heart failure, compared with 1325 (1%) of 166 228 matched controls over 8·3 years. This gave a hazard ratio (HR) of 4·69 (95% CI 3·64–6·04), after adjustment for time-updated age, sex, time-updated diabetes duration, birth in Sweden, educational level, and baseline comorbidities.

Worse glycaemic control was associated with increased risk of heart failure in a graded fashion, and so was the presence of albuminuria. Risk of heart failure was also increased among those with well controlled diabetes (adjusted HR 2·16 [95% CI 1·55–3·01]) and in those with no albuminuria (3·38 [2·51–4·57]), but not in the subgroup both well-controlled and with normoalbuminuria (1·59 [0·70–3·58]).

Interpretation

Individuals with type 1 diabetes had a four-times increase in the risk of being admitted to hospital with heart failure compared with population-based controls. Poor glycaemic control and impaired renal function substantially increased the risk of heart failure.

Rosengren, A et al. (2015). Long-term excess risk of heart failure in people with type 1 diabetes: a prospective case-control study. *The Lancet Diabetes & Endocrinology*, 3 (11), 876 - 885

Effect of meat intake on staging of diabetic chronic kidney disease

Chronic kidney disease (CKD) has a high prevalence, affecting 7.2% of the adult population worldwide. In most countries, diabetes mellitus, and particularly type 2 diabetes (T2D), has become the most frequent cause of chronic kidney disease.[1] Furthermore, due to the increasing prevalence of T2D, diabetes-related chronic kidney disease is presently the leading cause of end stage renal disease in many countries.[2]

International guidelines stress that accurate screening and staging of chronic kidney disease is pivotal in prevention and management.[3,4] Glomerular filtration rate (GFR) has been recognized as the best measure of kidney function, but its direct measurement by 'gold standard' inulin clearance or radio-isotopic methods, is not available in clinical practice. Estimation of GFR is thus recommended, using calculation based on creatinine plasma levels, age, sex, ethnicity, and body weight.[5,6] Misclassification of chronic kidney disease stage may result from variations of creatinine levels, with potential clinical implications. Some causes of variations are well known, and include muscle mass, fluid status and delay in centrifugation of blood. But also nutritional factors such as dietary protein intake[7], and in particular, creatine from meat, which is converted into creatinine by cooking and is absorbed, significantly increases creatinine plasma levels.

"the effect of cooked meat on creatinine levels disappeared after 12 hour fasting in all groups."

To evaluate the importance of these variations, the potential effects of intake of cooked meat on creatinine and eGFR were thus systematically assessed in control subjects without diabetes, and in people with diabetes in different stages of chronic kidney disease.[8] The effect of a standardized cooked meat meal was compared with that of a nonmeat meal (each providing 54 g of protein together with 250 ml water) on separate days. Samples for the creatinine assay were drawn in the fasting state, and at 1, 2, and 4 hours after test meal. Estimation of GFR (eGFR) was performed by the Modification of Diet in Renal Disease (MDRD) equation.

The study included 16 healthy volunteers, and 4 groups of 16 individuals with T1D and T2D and chronic kidney disease stages 1 to 4 (1-2, 3a, 3b, and 4). Compared with the fasting state, a significant increase in post prandial creatinine levels was observed in controls (6.7%) and in all groups of people with diabetes and chronic kidney disease (ranging from 7.5 to 17.5%). As a consequence, median eGFR decreased significantly, by 9.1% in controls and by 6.7 to 17.6% in all groups with diabetes, with a more marked effect in groups with less severe kidney function impairment (chronic kidney disease stages 1-2, and 3a).

The implication may have been important for management, as 6 out 16 individuals with chronic kidney disease stage 3a would have been misclassified as CKD 3b if blood samples had been drawn in postprandial rather than in the fasting state. Finally, the effect of cooked meat on creatinine levels disappeared after 12 hour fasting in all groups.

In conclusion, for determining creatinine plasma levels and eGFR, (which represent the most suitable routine tools together with urinary albumin excretion assay for chronic kidney disease screening and staging), blood sampling should be performed in the fasting state rather than at random.

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