Causes of Excess Mortality in Well Adjusted Type 2 Diabetes Mellitus Patients. Observations From a Mortality Follow-Up in a Cohort of Patients in a Type 2 Diabetes Mellitus Disease Management Program

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Submitted for Presentation at the European Population Conference 2016
Mainz August 31 – September 03, 2016

Introduction:
Alongside with the global obesity epidemics, Diabetes Mellitus Type 2 (T2DM) has become a pandemics. Primary and secondary prevention of Diabetes Mellitus Type 2, however, is crucial for preventing co-morbidity in advanced age and, therefore, for healthy aging and, therefore, for the demographic future of rich societies.

Today, the majority of T2DM cases in Rich Societies is diagnosed by screening lab tests, with no or at most subtle clinical symptoms present. Also, the majority of diagnosed T2DM cases (2/3 in Germany) is in some kind of managed care programs with regular visits to specialists, mostly with blood pressure values and long-time-glucose-in-blood (HbA1c) values considered normal, and mostly getting along with oral antidiabetic medication, without insulin injections. Still, age-standardized mortality in such well-adjusted patients is substantially higher than in subjects without the disease. Perhaps biomedical parameters considered "normal" in healthy subjects – that is: healthy individuals with even lower or higher (whatever is better) values than "normal" have no survival advantage – may be not optimal in diabetes patients, Here, the lower or the higher (whatever is better) such values, the better for the survival of patients. The results of the Systolic Blood Pressure Intervention Trial (SPRINT) point in this direction: the deeper the systolic blood pressure was lowered by aggressive medication, the lower was the all-cause mortality as well as the cardiovascular morbidity[1].

Data:
We do have a cluster-randomized, controlled intervention trial, a cohort with four waves, each six months apart, enclosing n=404 T2DM patients in a metropolitan area in South West Germany, all enrolled in a T2DM managed care program, aged 40-69 when recruited. First-Patient-In was in spring 2009, last-Patient-Out was in fall 2011. The intervention - feedback of a personalized risk profile for experiencing a Diabetes Mellitus typical complication within the next 10 years: Heart Infarction, Stroke, Kidney Failure, Blindness, Foot Amputation – proved to be ineffective. Therefore, for studying differential longevity, the two arms of the study can be considered an observation cohort. By the end of September 2015 we conducted an exploratory mortality-follow-up, tracing all original patients. We will repeat the mortality-follow-up by the end of 2015.

Results:
In September 2015, all-cause mortality (n=28+) was found to be threefold as high as expected in an age-adjusted sample of the general population. Although numbers are too small for studying single causes of death, by inspection Diabetes Mellitus typical complications dominate. For systolic blood pressure, fastening glucose and long-term glucose-in blood (HbA1c), as well as certain lipid values (Triglycerides, Total Cholesterol, Non-HDL-Non-LDL-Cholesterol, HDLChol, LDLChol), there seems to be a strictly monotonic association between levels of these risks factors and survival.

[1] http://www.nih.gov/news-events/news-releases/landmark-nih-study-shows-intensive-blood-pressure-management-may-save-lives

Discussion:
Clearly, number of events still is far too low to be sure, but the direction of eventual effects may be visible right now.

Conclusion:
In order to maximize survival, diabetes mellitus Type 2 patients should be managed not by guiding them within the borderlines of parameters considered “normal”, but by striving for optimal parameter values by aggressive disease management: the lower (or the higher – whatever applies) the respective risk parameter, the better. This general rule may also apply to other chronic conditions relevant for survival and health aging.