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The dynamics of life expectancy over the last six decades in elderly people with diabetes

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ABSTRACT

Aim: To investigate the historical changes in survival with diabetes in elderly people with diabetes.

Research design and methods: We analyzed 6504 deaths (44.5% males) registered in a large urban population, aged ≥65 years, and deceased between 1943 and 2009. We split the analysis into three time periods according to year of death: 1943–1965, 1966–1988 and 1989–2009. The parallel changes in the corresponding general population were available.

Results: The mean age at diabetes onset was 70.8 ± 4.7 years, with mean disease duration at death 7.5 ± 5 years, and mean age at death 78.3 ± 5.9 years. The mean survival loss due to diabetes (expected minus observed survival) was 4.5 ± 5.1 years (4.9 ± 5.1 years for females versus 4.1 ± 5.2 years for males, $p < 0.001$). The mean disease duration at death was 6.4 ± 5.7 years in the period 1943–1965, followed by a significant ($p = 0.019$) rise to 7 ± 5 years in 1966–1988, and 8.3 ± 4.9 years ($p < 0.001$) in 1989–2009. There was a significant increase in coronary heart disease and stroke, and a significant decrease in infections and end-stage renal disease as causes of death.

Conclusions: We found a significant increase in age at onset and survival with diabetes leading to a significant increase in age at death. Females had a higher survival loss due to diabetes compared with males.

1. Introduction

Diabetes mellitus is one of the most common chronic diseases and a major health problem in nearly every country. Its prevalence has risen sharply worldwide during the past few decades [1,2], an increase mainly explained by the epidemics of obesity and, consequentially, type 2 diabetes. Moreover, predictions for the next 20 years show that diabetes prevalence will continue to rise, reaching 7.7% (439 million adults worldwide) by 2030 [3]. Numerous studies have shown higher mortality rates in people with type 2 diabetes compared with the general population, mostly explained by cardiovascular events [4,5]. It is hoped that mortality rates in type 2 diabetes patients will be reduced as a result of major progresses in the treatment of hyperglycemia, hypertension, dyslipidemia and other cardiovascular risk factors [6]. However, a recent meta-analysis showed that intensive glucose control has no impact on mortality [7]. It is likely that other, overlooked factors are implicated in explaining this phenomenon.

The aim of this study was to analyze the dynamics of survival after diabetes onset in elderly people deceased between 1943 and 2009 in Bucharest, Romania. To our best knowledge, this is the first report of mortality in elderly people with diabetes in Romania. The survival dynamics of Romanian

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Abbreviations: BMI, body mass index; CHD, coronary heart disease; ESRD, end stage renal disease; FBG, fasting blood glucose.

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young adult type 1 diabetes and adult type 2 diabetes patients were previously reported elsewhere [8,9].

2. Patients and methods

2.1. Study population

The Bucharest Diabetes Registry was founded by Prof. Ion Pavel in 1941 and continues to the present day, making it one of the oldest regional diabetes registries in Europe. It includes nearly all patients discovered with diabetes in the area because this was the only site were diabetes medication was available (free of charge). From 2006 medication started to be distributed by all regular pharmacies and some patients were probably lost from the Registry because of the less tight control of provided treatment. Nonetheless, the representativeness of our cohort remains extremely high because most of the new diabetes care providers report their subjects to the central Diabetes Registry on a monthly base. This is a retrospective study of deaths recorded at the Bucharest Diabetes Centre between 1943 and 2009 in elderly people with diabetes, aged $\geq$65 years at diabetes onset.

The inclusion criteria were: patient registered at Bucharest Diabetes Centre, and deceased between 1943 and 2009. The exclusion criteria were: an age of less than 65 years at diabetes onset; residency outside Bucharest; lack of basic information such as gender or age at diabetes onset (i.e. missing medical records).

2.2. Confounders

For each subject the following data were recorded: sex, age at diabetes onset, disease duration, age at death, cause of death, year of death and insulin treatment anytime during life. The following supplemental data were available for a subgroup (by availability of data in the medical records): height, weight and estimated mean fasting blood glucose. Both weight and height were measured at first registration at the Centre, which can differ from diabetes diagnosis with an estimation of two months for the period 1943–2009 (more at the beginning and less in the recent years). Body mass index (BMI) was calculated as: weight (kg)/height^2 (m). Mean fasting blood glucose (FBG) was roughly estimated based on laboratory values recorded in patients' files, from registration to end of follow-up/death (around two determinations for each year). Although this is a poor indicator of metabolic control we decided to keep it because we already had a limited number of descriptive variables and it had an added value in some analysis. Glycated hemoglobin was not available on a large scale until 2000. Cause of death was based on that stated in the death certificate. Diabetes was noted as a cause of death when no other cause was found and the patient was known to have diabetes. Diabetic coma was recorded apart from diabetes as a cause of death, but no further information regarding hypo- or hyperglycemia was available.

2.3. Control group

The control group was constructed using data for the corresponding general population available from the National Institute of Statistics [10]. Historical data was available for years 1967, 1961, 1956 and 1932 as census data. From 1970 onwards, details such as mean age at death were available, and the full exposed population and registered deaths was available from 1990, as yearly measured data [10]. Data for the missing years was extrapolated (mostly by last observation carried backwards) from the available data.

2.4. Statistical analysis

Statistical analyses used parametric and nonparametric tests according to the data set. Assessment of the differences between two groups was performed using Student t, Mann–Whitney/Wilcoxon or χ^2 test as appropriate. All p values were two-tailed and statistical significance was defined as $p < 0.05$. Continuous variables are presented as mean $\pm$ standard variation. Due to the inevitable changes in mortality during such a large period of time, we detailed the survival analysis using three relatively equal time periods according to the year of death: 1943–1965, 1966–1988 and 1989–2009. Cut-off points were also chosen based on two major historical events with profound implications in all aspects of life: (a) the beginning of Ceausescu's communist regime in 1965, and (b) its end in 1989 by the Romanian Revolution, which introduced the democracy. The proportional hazard (Cox) regression was performed using the following available risk/protection factors for mortality:

1. Gender – female compared with male.
2. Age at diagnosis – effect of 1 year increase.
3. Body mass index – effect of 1 kg/m^2 increase.
4. Mean fasting plasma glucose – effect of one mmol/L increase.
5. Time period of death – 1989–2009 as reference period.

Cox regression analysis retained a significant model (Omnibus tests of model coefficients: $p < 0.001$) containing age at diagnosis, mean fasting plasma glucose and time period of death. Gender and body mass index did not reach statistical significance and were excluded from the model. Body mass index and fasting plasma glucose were not available as discrete values throughout the time and therefore a time-dependent analysis could not be performed.

The study was approved by the local ethics committee.

3. Results

We analyzed 6504 deaths, 2893 (44.5%) males and 3611 (55.5%) females registered at the ''I. Pavel'' Bucharest Diabetes Centre, and respecting all the inclusion and exclusion criteria mentioned above. The mean age at diabetes onset was 70.8 $\pm$ 4.7 years (71 $\pm$ 4.7 years for females versus 70.6 $\pm$ 4.6 years for males, $p = 0.001$), with a mean diabetes duration at death of 7.5 $\pm$ 5 years (7.7 $\pm$ 5.0 years for females versus 7.3 $\pm$ 5.1 years for males, $p = 0.01$) and mean age at death of 78.3 $\pm$ 5.9 years (78.6 $\pm$ 5.8 for females versus 77.9 $\pm$ 6.0 years for males, $p < 0.001$).

Based on the general population data, the mean expected survival at the moment of diabetes onset was 12.1 $\pm$ 2.6 years