Prediction of Mortality in Type 2 Diabetes from Health Related Quality of Life (ZODIAC-4).

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ABSTRACT

Objective: To investigate the relationship between health related quality of life (HRQOL) and mortality in type 2 diabetes.

Research Design And Methods: In 1998, 1143 primary care patients with type 2 diabetes participated in the ZODIAC study. At baseline, HRQOL was assessed with the RAND-36 and after almost 6 years life status was retrieved. Cox proportional Hazard modeling was used to investigate the association between HRQOL (continuous data) and mortality, with adjustment for selected confounders (smoking, age, sex, diabetes duration, HbA1c, renal function, BMI, blood pressure, cholesterol/HDL and macrovascular complications).

Results: The Physical Component Summary of the RAND-36 was inversely associated with mortality (HR: 0.979, 95%CI: 0.966 to 0.992), as were two separate RAND-36 dimensions.

Conclusions: This study found that HRQOL is an independent marker of mortality and emphasizes the importance of looking beyond clinical parameters in patients with type 2 diabetes.
Amongst others, hypertension and dyslipidemia are well known clinical risk factors in type 2 diabetes, which should be treated accordingly (1). However, studies in non-diabetic populations have also found that factors like worse health related quality of life (HRQOL) are associated with higher mortality (2-4). If this holds true for patients with type 2 diabetes, clinicians might have to give more attention to HRQOL and perhaps assess HRQOL routinely in these patients. This study is to our knowledge the first one investigating the relationship between HRQOL and mortality in type 2 diabetes.

**RESEARCH DESIGN AND METHODS**

In 1998, 1143 primary care patients with type 2 diabetes participated in the ZODIAC-study (5). Patients with serious co-morbidity, or impaired cognitive abilities were excluded (n=57). Baseline data involved a full medical history including macrovascular complications, diabetes duration, body mass index (BMI) and tobacco consumption. Laboratory and physical assessment data were collected and included HbA1c, non-fasting lipid profile, serum creatinine, albuminuria, blood pressure, weight and height. This study was approved by the local medical ethics committee.

HRQOL was measured with the RAND-36 (6). The RAND-36 contains 9 health dimensions. To interpret the overall direction of the HRQOL effects, two summary measures can be calculated: the physical (PCS) and mental (MCS) component summary. Scores are from 0-100; higher scores indicate better HRQOL.

Life status in 2004 and cause of death were retrieved from records maintained by the hospital and general practitioners. Ten baseline variables were selected for their possible confounding effects in the relationship between HRQOL and mortality, i.e., smoking (yes or no), age, sex, diabetes duration, HbA1c, renal function (estimated with Cockcroft-Gault), BMI, blood pressure, cholesterol/HDL and macrovascular complications (yes or no).

Cox proportional Hazard modeling was used to investigate the association between HRQOL (continuous data) and mortality, with adjustment of selected confounders. For Kaplan Meier curves, HRQOL scores were dichotomized.

**RESULTS**

In the study population there were 653 women (57%). Mean (standard deviation) age at baseline was 68.2 (11.5) years, median (P25-P75) diabetes duration 6 (3-11) years. Median follow-up time was 5.8 years. At follow-up, 335 patients had died, 101 of cardiovascular causes. Date of death was known in 329 (98%) patients.

Data on HRQOL were available from 1000 (87%) patients, and complete in 857 (75%) cases. Completeness of data was inversely associated with mortality (Hazard Ratio (HR) 0.355, 95% confidence interval (CI): 0.272 to 0.462 for 1 to 8 missing scales; HR 0.549, 95%CI: 0.382 to 0.788 for all 9 scales missing compared to complete data).

The PCS score was inversely associated with mortality (HR: 0.979, 95%CI: 0.966 to 0.992). A decrease of 1 point on the PCS score led to an increase of the hazard of mortality of 2.1%. 145 (32.4%) of 448 patients with PCS scores below the median died versus 69 of 449 (15.4%) with PCS scores above the median (a 2.1 ratio) (Figure 1).

The MCS score was not associated with mortality (HR 1.008, 95%CI: 0.994 to 1.022).

For separate RAND-36 dimensions, significant relationships were found for “Physical Functioning” (HR 0.989, 95%CI: 0.982 to 0.996) and “General Health Percepcion” (HR 0.982, 95%CI: 0.971 to 0.994).

For cardiovascular mortality, results remained significant for “Physical Functioning” (HR 0.987, 95%CI: 0.977 to 0.996). HRs for “General Health
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Perception” and PCS were 0.967 (95%CI: 0.967 to 1.000) and 0.982 (95%CI: 0.964 to 1.001), respectively.

CONCLUSIONS

Worse HRQOL is associated with higher overall mortality in patients with type 2 diabetes in 6 year follow-up, after taking potential confounders into account. Patients with low versus high HRQOL (PCS score) have a 2.1-fold increased mortality risk. Two separate RAND-36 dimensions; “Physical Functioning” and “General Health Perception” were related to mortality. The former has questions about ability to perform physical activities, the latter questions about patients’ opinion about their health in general. “Physical Functioning” was also associated with cardiovascular mortality.

Limitations of this study were that 25% of patients did not fill in or complete the questionnaire. However, this was strongly related to mortality and has therefore probably led to an underestimation of the effects of HRQOL on mortality (7). Of course, confounders other than the 10 selected in this study could influence the prediction of mortality from HRQOL; for example depression, which is more prevalent in type 2 diabetes, is related to worse HRQOL and mortality(8). Furthermore, it is important to emphasize that an association between HRQOL and mortality does not establish causality.

Nevertheless, this study emphasizes that in patients with type 2 diabetes it is important to look beyond clinical parameters. Good HRQOL is an important goal of health care in itself. Yet, demonstrating that HRQOL is an independent marker of mortality in type 2 diabetes provides an added incentive for health care providers to assess HRQOL routinely in diabetes care, allowing any underlying unmet needs to be identified and, where possible, addressed. Research is needed to examine if the association reflects specific modifiable risks, rather than overall disease burden.

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REFERENCES

FIGURE LEGEND

FIGURE 1. Kaplan-Meier curve Physical Component Summary