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

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

RESEARCH DESIGN AND METHODS — In 1998, 1,143 primary care patients with type 2 diabetes participated in the Zwolle Outpatient Diabetes project Integrating Available Care (ZODIAC) study. At baseline, HRQOL was assessed with the RAND-36 and, after almost 6 years, life status was retrieved. Cox proportional hazards modeling was used to investigate the association between HRQOL (continuous data) and mortality with adjustment for selected confounders (smoking, age, sex, diabetes duration, A1C, renal function, BMI, blood pressure, HDL cholesterol, and macrovascular complications).

RESULTS — The Physical Component Summary of the RAND-36 was inversely associated with mortality (hazard ratio [HR] 0.979 [95% CI 0.966–0.992]), 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.

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Among others, hypertension and dyslipidemia are well-known clinical risk factors in type 2 diabetes and should be treated accordingly (1). However, studies in nondiabetic 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, 1,143 primary care patients with type 2 diabetes participated in the Zwolle Outpatient Diabetes project Integrating Available Care (ZODIAC) study (5). Patients with serious comorbidity or impaired cognitive abilities were excluded ($n = 57$). Baseline data involved a full medical history including macrovascular complications, diabetes duration, BMI, and tobacco consumption. Laboratory and physical assessment data were collected and included A1C, nonfasting 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 nine 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 range 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, A1C, renal function (estimated with Cockcroft-Gault), BMI, blood pressure, HDL cholesterol, 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

— The study population included 653 women (57%). Mean ± SD age at baseline was 68.2 ± 11.5 years with median diabetes duration 6 years (interquartile range 3–11). Median follow-up time was 5.8 years. At follow-up, 335 patients had died, 101 from cardiovascular causes. Date of death was known in 329 (98%) patients.

Data on HRQOL were available from 1,000 (87%) patients and complete for 857 (75%) patients. Completeness of data was inversely associated with mortality (HR 0.355 [95% CI 0.272–0.462] for one to eight missing scales; 0.549 [0.382–0.788] for all nine missing scales compared with complete data).

The PCS score was inversely associated with mortality (HR 0.979 [95% CI 0.966–0.992]). A decrease of 1 point on

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Abbreviations: HRQOL, health-related quality of life; MCS, mental component summary; PCS, physical component summary, ZODIAC, Zwolle Outpatient Diabetes project Integrating Available Care.

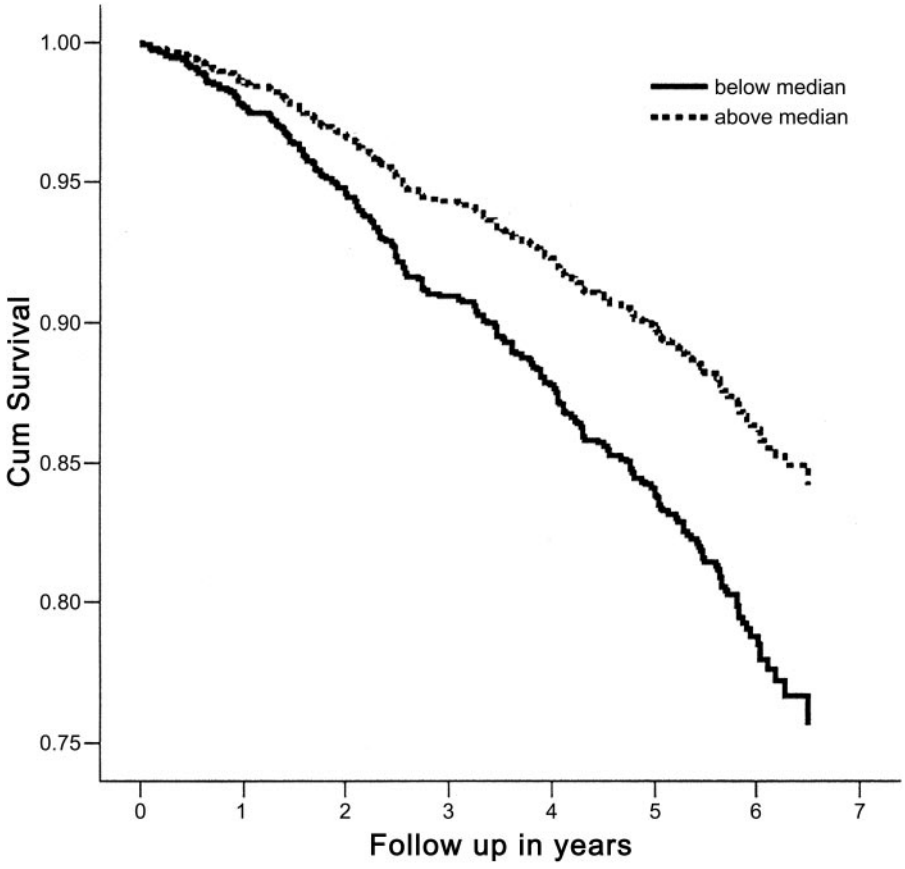

Figure 1—*Kaplan-Meier curve PCS.*

the PCS score led to an increase of the hazard of mortality of 2.1%. A total of 145 (32.4%) of 448 patients with PCS scores below the median died vs. 69 of 449 (15.4%) with PCS scores above the median (a 2.1 ratio) (Fig. 1). The MCS score was not associated with mortality (1.008 [0.994–1.022]).

For separate RAND-36 dimensions, significant relationships were found for "physical functioning" (HR 0.989 [95% CI 0.982–0.996]) and "general health perception" (0.982 [0.971–0.994]).

For cardiovascular mortality, results remained significant for physical functioning (HR 0.987 [95%CI 0.977–0.996]). HRs for general health perception and PCS were 0.967 [95% CI 0.967–1.000] and 0.982 (0.964–1.001), 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, e.g., depression, which is more prevalent in type 2 diabetes, is related to worse HRQOL and higher 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 addressed when possible. Further research is needed to examine if the association reflects specific modifiable risks rather than overall disease burden.

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