Erectile Dysfunction and Quality of Life in Type 2 Diabetic Patients

A serious problem too often overlooked

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OBJECTIVE — Within the context of a large, nationwide outcomes research program in type 2 diabetes, we assess the prevalence of self-reported erectile dysfunction and evaluate its impact on quality of life.

RESEARCH DESIGN AND METHODS — The study involved 1,460 patients enrolled by 114 diabetes outpatient clinics and 112 general practitioners. Patients were asked to complete a questionnaire investigating their ability to achieve and maintain an erection. Various aspects of quality of life were also assessed depressive using the following instruments: SF-36 Health Survey, diabetes health distress, psychological adaptation to diabetes, depressive symptoms (CES-D scale), and quality of sexual life.

RESULTS — Overall, 34% of the patients reported frequent erectile problems, 24% reported occasional problems, and 42% reported no erectile problems. After adjusting for patient characteristics, erectile dysfunction was associated with higher levels of diabetes-specific health distress and worse psychological adaptation to diabetes, which were, in turn, related to worse metabolic control. Erectile problems were also associated with a dramatic increase in the prevalence of severe depressive symptoms, lower scores in the mental components of the SF-36, and a less satisfactory sexual life. A total of 63% of the patients reported that their physicians had never investigated their sexual problems.

CONCLUSIONS — Erectile dysfunction is extremely common among type 2 diabetic patients and is associated with poorer quality of life, as measured with generic and diabetes-specific instruments. Despite their relevance, sexual problems are seldom investigated by general practitioners and specialists.

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Erectile dysfunction (ED) is a common complication of diabetes; the reported prevalence ranges from 35 to 70% (1–8). In the Massachusetts Male Aging Study (9), the age-adjusted probability of complete impotence was three times greater (28%) in patients with treated diabetes than in those without diabetes (9.6%). In addition to its higher frequency, ED also occurs at an earlier age in the diabetic population as compared with the general population (1–10) and is often related to duration and severity of diabetes (4,5,8).

Although psychogenic factors, such as performance distress, can contribute to its etiology, ED in diabetic patients is mainly related to organic causes, such as vasculogenic and neurological abnormalities (11,12). The presence of a normal sexual desire and the inability to physically act on that desire can affect patients' lives in different ways, including disorders in interpersonal relationships, interference with sexual life, problems with partners, and increase in mental stress, making ED a major quality of life (QoL) issue (13). Recent pharmacological advances have stimulated a great interest in ED, generating new data concerning its prevalence (4,5,7–9,14), treatment (15,16), and costs (17,18). Nevertheless, even in randomized clinical trials, little attention has been given to QoL. Instead, attention has been focused mainly toward evaluation on patient and partner satisfaction for sexual life (19–21). Furthermore, most of the data from both randomized trials and observational studies do not refer specifically to patients with diabetes (22,23). Therefore, little is known about the impact of this complication on broader measures of subjective well-being and QoL, particularly among patients with type 2 diabetes, for whom only few data derived from small samples are available (24).

Within the context of the QuED project, a nationwide outcomes research program aimed at assessing the relationship between the quality of care delivered to patients with type 2 diabetes and a wide array of outcomes, we estimated the prevalence of self-reported ED and evaluated its impact on QoL, as assessed by generic and disease-specific instruments.

RESEARCH DESIGN AND METHODS

Population and data collection

Patients were enrolled by 114 diabetes outpatient clinics and 112 general practi-

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Abbreviations: CES-D, Center for Epidemiological Studies-Depression; ED, erectile dysfunction; QoL, quality of life.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

tioners. Physicians in all regions of Italy were identified and selected according to their willingness to participate in the project. All patients with type 2 diabetes were considered eligible for this project, irrespective of age, duration of diabetes, and treatment. In diabetes outpatient clinics, patients were sampled by using random lists, stratified by patient age (<65 or ≥65 years). Each center was asked to recruit at least 30 patients, whereas general practitioners enrolled only those patients for whom they were primarily responsible for diabetes care. Patients were scheduled to be followed for 5 years, and information was to be collected at 6-month intervals. We report here a cross-sectional evaluation, based on baseline patient data.

General medical history and diabetes-specific data were collected by the patients' physicians using forms specifically developed for the project by the scientific committee. For all clinical variables, the last value in the previous 12 months was requested. Because normal ranges for glycated hemoglobin varied among the different centers, the percentage change with respect to the upper normal value (actual value/upper normal limit) was estimated and multiplied by 6.0.

All subjects were asked to complete a questionnaire upon entry into the study and at 6-month intervals over a period of 3 years. The questionnaire was self-administered and then sent anonymously to the coordinating center in prepaid envelopes. Prevalence of ED was determined by asking the patient how often he had experienced problems in attaining and maintaining an erection during the past 6 months, with responses calibrated on a five-level scale (from never to more than once per week). Patients were then grouped into three classes, according to reported frequency of ED: never, occasionally (once per month or less), or frequently (almost every week or more than once per week). For the purposes of our analyses, we considered only those patients who reported frequent erectile problems as affected by ED.

The presence and severity of diabetes complications and comorbidities were summarized by using the Total Illness Burden Index, a widely used comorbidity measure specifically developed for outpatient populations (25). This index can be used as a continuous measure or categorized in four classes of increasing severity.

The questionnaire also investigated how often in the past 12 months the doctor in charge of diabetes care had asked the patient about problems with his sex life. Answers were given on a five-point scale ranging from "at every visit" to "never."

QoL measures

QoL was assessed using generic and diabetes-specific measures. The latter were developed in the framework of the Diabetes Outcomes Research Project (PORT)-Diabetes 2 (26).

SF-36 Health Survey

The SF-36 Health Survey is one of the most widely used measures of health-related QoL and consists of 36 items covering eight dimensions: physical functioning (PF), role limitations caused by physical health problems (RF), bodily pain (BP), general health perception (GH), vitality (VT), social functioning (SF), role limitations caused by emotional health problems (RE), and mental health (MH) (27). Scores on all the subscales are transformed linearly to a possible range of 0–100; higher scores indicate more favorable physical functioning/psychological well-being.

CES-D Scale

The CES-D Scale is a self-reported measure of depression that is widely used in various settings and patient populations. It is composed of 20 items addressing symptoms of depression during the previous 4 weeks. Symptom frequency is rated from "none of the time" to "most or all of the time" on a four-point Likert scale (28). Values of the Center for Epidemiological Studies-Depression (CES-D) Scale range from 0 to 60; values ≥16 indicate the presence of depressive symptoms (29). In a sample of elderly inpatients, the sensitivity of such a cutpoint was 73% for any depression and 90% for major depression; the associated specificity was 84% in both cases (30). More recently, a CES-D score ≥21 has been proposed for the screening of major depression in outpatient elderly subjects, yielding a sensitivity of 92% and a specificity of 87% (31).

Diabetes-related stress

Composed of eight items, the diabetes-related stress scale is derived from the questionnaire developed by Dunn et al. (32) and investigates the psychological adaptation to and acceptance of diabetes. In particular, this scale assesses feelings of being "different" and leading a different lifestyle, of living under a life sentence, and of diabetes being "the worst thing that ever happened." Answers are given on a five-point Likert scale, ranging from "strongly disagree" to "strongly agree." The scores range from 0 to 100, and higher scores indicate higher levels of stress.

Diabetes health distress

The diabetes health distress scale is composed of five items and explores the extent to which diabetes can be a source of frustration, discouragement, nuisance, or concern. Patients are asked how often in the past 4 weeks diabetes was responsible for such feelings, and answers are given on a five-point Likert scale, ranging from "all of the time" to "none of the time." Responses are scaled from 0 to 100, and higher scores represent higher levels of distress.

Sexual life questionnaire

The sexual life questionnaire comprises six items used to explore quality of sexual life. Subjects are asked to score how much the following aspects influenced their sexual life: problems connected to overall physical health, diabetes, tension or stress, fatigue or lack of energy, general lack of interest in sex, and problems specifically due to gallbladder disease or treatment. Answers are rated from "a great deal" to "not at all" on a five-point Likert scale. Scores are scaled from 0 to 100, and a higher score indicates a better quality of sexual life.

Except for the SF-36 Health Survey, largely used in the Italian population (33), all the instruments were translated, cross-culturally adapted, and validated in Italian specifically for the QuED study. Results relative to the validation process for CES-D, diabetes health distress, and diabetes-related stress have been reported elsewhere (34). All three scales showed excellent psychometric characteristics; for all scales, the Cronbach's α-coefficient largely exceeded the minimum accepted value of 0.70 (stress 0.81, distress 0.91, CES-D 0.89).

Statistical analysis

Patient characteristics according to ED frequency were compared using the χ^2 test. When a continuous variable was categorized in more than two levels, the χ^2

Table 1—*Characteristics of the study population according to the frequency of ED* (n = *1,460)*

Characteristics	Frequency of ED			*P*
	Never	Occasionally	Frequently	
n	615	346	499	
Age (years)				0.001
≤55	205 (61)	68 (20)	64 (19)	
56–65	224 (42)	145 (27)	168 (31)	
>65	160 (31)	121 (23)	243 (46)	
School education (years)				0.01
≤5	259 (49)	120 (23)	154 (29)	
6–8	169 (38)	106 (24)	166 (38)	
9–13	131 (38)	87 (25)	130 (37)	
>13	43 (39)	27 (25)	39 (36)	
Marital status				0.9
Single/widow	93 (43)	48 (22)	74 (34)	
Married	522 (42)	298 (24)	425 (34)	
BMI (kg/m^2)				0.6
≤25	149 (39)	97 (25)	137 (36)	
25.1–27	132 (45)	67 (23)	94 (32)	
>27	298 (43)	161 (23)	234 (34)	
Smoking				0.01
No	160 (47)	76 (22)	103 (30)	
Yes	148 (45)	88 (27)	96 (29)	
Ex	293 (39)	175 (23)	287 (38)	
Duration of diabetes (years)				0.001
≤5	217 (49)	113 (25)	114 (26)	
6–10	140 (43)	76 (23)	113 (34)	
>10	192 (35)	132 (24)	228 (41)	
HbA_{1c} (%)				0.01
≤6.0	155 (46)	80 (24)	99 (30)	
6.1–8.0	257 (42)	143 (24)	207 (34)	
>8.0	111 (38)	73 (25)	112 (38)	
Diabetes treatment				0.001
Diet alone	138 (55)	69 (27)	46 (18)	
Oral agents	374 (42)	208 (24)	303 (34)	
Insulin	46 (29)	35 (22)	75 (48)	
Insulin + oral agents	30 (30)	22 (22)	49 (49)	
Total Illness Burden Index				0.001
Class 1	253 (56)	93 (21)	107 (24)	
Class 2	127 (39)	103 (31)	98 (30)	
Class 3	141 (39)	84 (23)	138 (38)	
Class 4	94 (30)	66 (21)	156 (49)	
Hypertension				0.002
No	384 (46)	198 (24)	259 (31)	
Yes	231 (37)	148 (24)	240 (39)	
Symptomatic neuropathy				0.001
No	583 (44)	317 (24)	427 (32)	
Yes	32 (24)	29 (22)	72 (54)	

Data are *n* (%).

Mantel-Haenszel test for linear association was applied. Values of continuous variables and QoL scores across classes of ED frequency were compared using the Kruskall-Wallis one-way analysis of variance, and correlation was estimated by the Pearson correlation coefficient. The impact of ED on QoL was also evaluated using a series of multiple regression analyses with stepwise variable selection. In these analyses, the eight dimensions of the SF-36 Health Survey and the other above-mentioned scales were considered as dependent variables, whereas patient characteristics were used as covariates. Because depression could represent a confounder of the relationship between ED and QoL, a series of multiple regression analyses including the CES-D score among the covariates was also performed. The following covariates were tested: age, duration of diabetes, Total Illness Burden Index, HbA_{1c} (all tested as continuous variables), years of school education (≤5 [reference category] or >5), marital status (married [reference category] or single/widowed), and diabetes treatment (diet ± oral agents [reference category], insulin only, or insulin + oral agents). The association of ED with the aforementioned scales is expressed in terms of β-parameters.

The sexual life questionnaire was validated using a multitrait multi-item method (35). This method is used to determine whether each item in a scale is substantially related ($r \geq 0.40$) to the total score computed from the other items in that scale (item-convergent validity criterion). Internal consistency reliability was estimated by the Cronbach's α-coefficient. Furthermore, the percentages of respondents achieving either the highest score (ceiling) or lowest score (floor) were calculated.

RESULTS

Prevalence

Of 3,564 patients with type 2 diabetes recruited for the QuED project, a total of 2,962 baseline questionnaires were returned (response rate 83%). The study population comprised male respondents (n = 1,620) who also reported the frequency of ED (n = 1,460 [90%]). The mean (±SD) age of the study population was 62 (±10) years. A total of 37% of the patients had completed ≤5 years of school education, 85% were married, and the mean duration of diabetes was 10 (±9) years.

Overall, 615 respondents (34%) reported frequent ED, 346 (24%) reported occasional ED, and 499 (42%) reported no erectile problems. Respondents' characteristics according to the reported ED frequency are shown in Table 1. Prevalence of ED in our study population was associated with patient age, duration of diabetes, worse metabolic control, history of smoking, treatment of diabetes, presence and severity of diabetes complications, and comorbid conditions (Table 1).

Table 2—*QoL scale scores according to ED frequency*

Scales	Frequency of ED			Pearson correlation coefficient
	Never	Occasionally	Frequently	
SF-36 Physical functioning	84.3 ± 18.8	80.6 ± 20.6	74.2 ± 23.8	−0.19
SF-36 Role physical	74.3 ± 36.6	69.9 ± 37.9	56.5 ± 43.3	−0.19
SF-36 Bodily pain	77.8 ± 23.9	72.4 ± 25.7	66.8 ± 26.5	−0.17
SF-36 General health	61.2 ± 18.9	58.7 ± 18.5	50.9 ± 20.3	−0.22
SF-36 Vitality	66.6 ± 19.0	63.2 ± 18.0	56.0 ± 20.7	−0.22
SF-36 Social functioning	77.6 ± 23.3	74.8 ± 22.2	66.2 ± 26.1	−0.20
SF-36 Role emotional	75.2 ± 36.4	71.4 ± 38.7	56.4 ± 43.1	−0.21
SF-36 Mental health	73.1 ± 18.3	69.9 ± 17.6	64.7 ± 21.3	−0.18
Diabetes health distress	26.2 ± 24.1	29.2 ± 22.6	38.8 ± 26.4	0.22
Diabetes-related stress	43.5 ± 19.6	45.9 ± 18.1	50.0 ± 20.7	0.14
Sexual life	87.3 ± 15.5	73.7 ± 17.5	61.8 ± 23.4	−0.44
CES-D	16.1 ± 8.9	18.9 ± 9.3	20.1 ± 10.2	0.15

Data are means ± SD. $P < 0.0001$ for all the differences (Kruskall-Wallis one-way analysis of variance and Pearson correlation coefficient).

These findings agree with the existing scientific literature on ED (4,9).

QoL evaluation

Validation of the Italian version of the sexual life questionnaire showed that the instrument has excellent psychometric characteristics, with a Cronbach's α-coefficient of 0.83, manifestly exceeding the minimum accepted value of 0.70 (36). The percentage of patients providing responses for every item in the scale was 86%, and for all items, the item-scale correlation was higher than the 0.40 accepted standard (range 0.50–0.71). Less than 1% of the patients scored at floor and 16.9% scored at ceiling.

Examination of the mean scores revealed a close relationship between the presence of ED and a worse subjective perception of health status, for all dimensions assessed by both specific and generic instruments. In particular, patients with ED had lower scores (i.e., worse QoL) in all the SF-36 subscales (Table 2); greater differences were seen for role physical, role emotional, and social functioning dimensions.

Likewise, men with self-reported ED showed significantly higher levels of diabetes-specific health distress, worse psychological adaptation to diabetes, and a less satisfactory sexual life (Table 2).

ED was also associated with higher CES-D scores: 45.6% of patients with frequent ED reported severe depressive symptoms (i.e. CES-D scores ≥21). Corresponding figures for those with occasional ED were 42.4 and 29.6% in the remainder ($\chi^2_{MH} = 29.8$, $P = 0.001$). The relative proportions of patients with scores ≥16 were 62.5, 60.6, and 47.2%, respectively ($\chi^2_{MH} = 26.0$, $P = 0.001$).

The analysis of the individual items of the sexual life questionnaire showed that 50% of the patients with ED considered diabetes to have a great impact on their sexual life, whereas one third (31%) regarded its presence as irrelevant. Among the other factors examined, overall physical health conditions (38%) and general lack of interest in sex (28%) were those more frequently considered to heavily influence sexual life.

Overall, only 10.1% of the patients (13.5% among those with ED) reported that their doctors had asked them at every visit/almost every visit about their sexual problems, whereas 63% declared that their physicians had never investigated these aspects. No major differences were seen between settings of care (62% among patients attending diabetes outpatient clinics and 66% among those in the charge of general practitioners; $\chi^2 = 2.2$, $P = 0.3$).

The results of multivariate analyses adjusted for patient characteristics showed that the presence of ED was significantly associated with all the QoL dimensions explored (Table 3). When the CES-D score was included as a covariate in the models, ED still remained an independent correlate of diabetes-related stress, diabetes health distress, sexual life questionnaire, and the mental health subscales of the SF-36. On the other hand, the association with the physical components of the SF-36 was no longer significant, showing that depression was an important confounder for the correlation between ED and physical functioning but not for its association with psychological well-being (Table 3).

Multivariate analyses also revealed an independent association between higher levels of HbA_{1c} and diabetes-specific health distress ($\beta = 1.14$, $P = 0.005$) and poor psychological adaptation to diabetes

Table 3—*β-parameters associated with ED in multiple regression analyses with each dimension of QoL as dependent variable*

QoL dimension	Multiple regression model without CES-D score as a covariate		Multiple regression model with CES-D score as a covariate	
	β	*P*	β	*P*
SF-36 Physical functioning	−2.65	0.03	−1.93	0.1
SF-36 Role physical	−7.47	0.002	−2.49	0.3
SF-36 Bodily pain	−5.59	0.0009	−2.52	0.09
SF-36 General health	−4.93	0.0001	−3.80	0.0004
SF-36 Vitality	−5.97	0.0001	−4.50	0.0001
SF-36 Social functioning	−5.79	0.0001	−3.02	0.01
SF-36 Role emotional	−11.84	0.0001	−9.36	0.0001
SF-36 Mental health	−6.93	0.0001	−3.32	0.0002
Diabetes health distress	10.99	0.0001	6.86	0.0001
Diabetes-related stress	3.30	0.006	2.37	0.03
Sexual life	−22.53	0.0001	−20.79	0.0001

Two sets of β-parameters are presented: the first relative to regression models not including CES-D values among the covariates, the second with CES-D values forced in the model.

($\beta = 1.18$, $P = 0.0004$). Both scales were also significantly associated with CES-D scores ($\beta = 0.96$, $P = 0.0001$ and $\beta = 0.61$, $P = 0.0001$, respectively).

We also performed all the previous analyses by taking the multilevel nature of the data into account (patients clustered within physician/practice). Nevertheless, as also described in a previous paper (34), the effect of setting-related characteristics on QoL scores was irrelevant and statistically not significant. Furthermore, the β-parameters relative to ED were not affected by the application of multilevel analyses.

CONCLUSIONS — To our knowledge, this is the largest study evaluating QoL in diabetic patients with ED. Subjects were recruited by a broad range of diabetes clinics and general practitioners reflecting different geographic areas and practice styles. Furthermore, the excellent psychometric properties of the instruments applied and the high response rate make our findings highly reliable and generalizable to the ambulatory population of patients with type 2 diabetes.

Our data show that ED is a very common problem, affecting one third of patients with type 2 diabetes, and that it is related to health status perception. A similar association has been found consistently with instruments covering a large array of QoL dimensions. In particular, patients with ED showed higher levels of frustration and discouragement and a lower acceptance of diabetes, which were, in turn, related to worse metabolic control and higher levels of depressive symptoms. These associations remained highly significant, even after adjusting the analyses for clinical and patient-related characteristics, thus excluding the possible confounding effect of other variables.

Another important finding of our study is the dramatic increase in the risk of depression given by the concomitant presence of diabetes and ED. In fact, in our sample, almost two thirds of the patients reporting ED also had CES-D values indicative of depressive symptoms. In the general male population of the Massachusetts Male Aging Study, involving 1,265 subjects aged 40–70 years (35% with ED), the percentage of patients with CES-D scores ≥16 remained <15% in all age strata (37). The prevalence of depressive symptoms in our patients with ED was also higher than that reported in previous studies of diabetic adults (38–41).

These findings are particularly important in light of the large body of evidence suggesting that depression, as measured by high CES-D scores, represents a risk factor for cardiovascular events (42–45), hypertension (46), and mortality (47).

It has been recently suggested that the effects of depressive symptoms, cardiovascular disease, and ED are mutually reinforcing (48). Although the cross-sectional nature of our analysis cannot clarify the causal link between depression and ED, it is important to stress that ED in men with diabetes is predominantly caused by organic factors. It is unlikely that the use of antidepressants and tranquilizers can account for our findings, because only a minority of patients were treated with these classes of drugs (2% of patients with ED were taking antidepressants and 6.8% were taking tranquilizers).

The hypothesis that depression might represent a confounder for the relationship between ED and other measures of psychological well-being was contraindicated by multivariate analyses. In fact, when CES-D score was added to the covariates, the β-parameters relative to the diabetes-specific measures and the mental components of the SF-36 showed only a moderate reduction with respect to the models not including CES-D scores, confirming their independent and statistically significant correlation with ED.

Although patients with ED confirmed our expectations in reporting a worse quality of sexual life, with diabetes and general health conditions considered the most common interfering factors, one third of the same patients reported that the impact of diabetes on their sexual lives was irrelevant. A general attitude of men with ED not to seek treatment because of ignorance, misinformation, and embarrassment has already been described (49). On the other hand, the tendency of physicians not to investigate sexual problems in diabetic patients and the need for clinician-initiated discussion regarding this issue have also been recently pointed out (50) and further confirmed by our data, which showed that two thirds of the patients were never asked about their sex lives in the past 12 months. Both general practitioners and specialists should thus increase their attention to sexual disorders, which are often not considered an important medical problem or are viewed as overshadowed by other medical conditions. Encouraging patients to openly discuss these problems could reassure them about the availability of successful and reasonably safe treatments. It would also allow an effective investigation, beyond sexual dysfunction, of the relevant additional risk of mainly cardiovascular morbidity and mortality conferred by the concomitant presence of ED and depression.

Two potential methodological limitations of our study must be discussed. The presence of ED was based on patient self-report, without any attempt to clinically confirm the diagnosis. Nevertheless, self-report techniques have been widely used to estimate the prevalence of sexual dysfunction (4,8,9,14), and our findings are highly consistent with previous data showing a prevalence of ED of 37% in an Italian population of >8,000 patients with type 2 diabetes (4). Furthermore, subjective evaluation of the individual' s erection and satisfaction for sexual life are more likely to influence psychological well-being rather than the objective evaluation of the degree of ED.

Second, the cross-sectional nature of our study does not allow us to draw definitive conclusions about the causal link between ED and QoL. These aspects will be further investigated in the longitudinal phase of the project, which is currently underway.

In conclusion, ED is negatively associated with an array of dimensions of psychological well-being. The strong association between sexual dysfunction and impaired QoL justifies recognition of ED in diabetic patients as a significant public health problem and calls for a much greater attention to the identification of patients suffering from ED. To this respect, sexual function should be considered an integral part of overall health in diabetic patients.

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APPENDIX

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