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Physical activity, dietary habits and cognitive decline in over 65 years Italian outpatients with type 2 diabetes: a cross-sectional pilot study

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This pilot study aims to assess the relations between lifestyle and cognitive decline (CD) and to describe the prevalence of CD in outpatients over 65 years with type 2 diabetes mellitus (T2DM), examining the feasibility of a future research endeavor. This was a single-center pilot study, using a cross-sectional data collection. Lifestyles, including dietary habits and physical activities, were examined. To measure lifestyles, we used a self-report questionnaire aimed to explore seven domains: weekly consumption of bread, pasta, red meat, fish, alcohol, daily consumption of coffee, and weekly physical activities. To measure CD, the mini mental state examination was used. For the role of lifestyles in explaining cognitive functions, a multivariate regression model was used, where the physical activities and the diet treatment were the only significant predictors of cognitive efficiency. The model explained the 24% of the cognitive functions variance, showing a residuals normal distribution and no collinearity. This pilot study has some important limitations related to the study design. Nevertheless, it provides preliminary information to assess the feasibility of a future research endeavor, confirming the importance of lifestyles to prevent the CD in subjects with T2DM and giving cues for future investigation.

Key words: Lifestyles, cognitive decline, diabetes, elderly

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Introduction

Diabetes mellitus is a common disease, affecting approximately 387 million people and rapidly increasing worldwide owing to the increasing occurrence of obesity and sedentary lifestyle.[1] Subjects with type 2 diabetes mellitus (T2DM) accounts for 85–90% of patients with diabetes.[1] The importance of T2DM in the health and social context is first owing to it being an established risk factor for cardiovascular disease, stroke, and peripheral vascular disease, all of which represent the paramount causes of mortality and morbidity in the industrialized countries.[2] For this reason, T2DM is becoming one of the largest challenges to health care systems.

Subjects with T2DM show a faster cognitive decline (CD) compared with healthy subjects.[3] Most of subjects with T2DM are over 65 years, and their lifestyles could be associated with the rate of CD, especially the dietary habits[4] and the physical activities.[5] Furthermore, physical activities and dietary habits are also known to delay or prevent the progression of prediabetes to T2DM.[6]

T2DM can surely affect the central nervous system,[7] and the literature suggests that diabetes also plays a role in accelerated brain aging.[8] The presence of gradual CD over several years prior to the diagnosis of dementia is well described.[9] CD and dementia affect 15% of those over the age of 65 years and up to 50% of those over the age of 85 years; furthermore, it is expected to increase more than 100% in incidence by the year 2050.[10] If T2DM increases risk of dementia even mildly, the public health implications could be very relevant.

The effect of T2DM treatment on the risk of CD is examined in different studies,[11,12] but there is no consensus about findings.[13] Regarding dietary habits, there are arguments suggesting that nutrients such as vitamins, trace minerals or lipids can affect the risk of CD, especially in elderly people at risk of deficiencies.[4] The literature also shows the association between level of glycemic control and subsequent rate of CD,[14,15] for this reason, dietary habits aimed to metabolic control are linked with the risk of CD. Moreover, the intensive glycemic control – aimed at achieving and maintaining glycaemia as close to normal as possible – does not beneficial effects on percentage of CD.[16] Rather, the subjects treated with intensive glycemic control present an increased rate of hypoglycemia than in subjects with standard glycemic control.[17] In addition, scientific evidence supports the importance of physical activities to reduce complications associated with T2DM.[18] Although it is known that T2DM may be associated with an increased risk of CD, mechanisms and mitigating factors do not

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remain entirely clear, and it is unclear how physical activities interact with the CD in patients with T2DM.

Moreover, there are almost 3 million people in Italy with diabetes and 90% of them have a T2DM, representing a 4.9% of overall Italian population.[19] The prevalence of T2DM increases with age, and 80 of 100 T2DM patients have more than 65 years.[19] However, there are no studies that investigate the prevalence of CD in Italian populations of T2DM patients.

The study

Aim

This pilot study aims to assess the relations between lifestyle and CD and to describe the prevalence of CD in outpatients over 65 years with T2DM, examining the feasibility of a future research endeavor.

Design

This was a single-center pilot study based on cross-sectional data. The study was conducted at Policlinico San Donato Hospital in Milan, between November 2014 and January 2015.

Participants

Study participants were outpatients over 65 years with T2DM. Exclusion criteria were: presence of more than two significant comorbidities (e.g. significant thyroid, renal, or hepatic diseases, advanced malignancies, active psychiatric illnesses, or substance abuse problems); incapacity to give informed consent; recent diagnosis of T2DM (<6 months); recent value of glycated hemoglobin (HbA1c) ≥ 7%.

Between November 2014 and January 2015, 120 patients who fulfilled the inclusion criteria were invited for the preliminary interview. Of these, 39 patients were excluded because of presence of more than two significant comorbidity ($n = 33$), unwillingness to be involved in the study ($n = 5$), and diagnosis of active psychiatric problems ($n = 1$; exclusion criteria). In the sample, 63% were male ($n = 51$), 80.2% were married ($n = 65$), only one was not an Italian, most had an education background lower than high school graduation (64.4%; $n = 53$). Patients treated with drugs associated with risk of hypoglycemia were 77.8% ($n = 63$). Furthermore, 77.8% were not smokers ($n = 63$), 71.6% had hypertension ($n = 58$), 42.0% had a diagnosed heart disease ($n = 34$), and 4.9% had a previous stroke in the last 5 years. Mean age was 74.2 ± 7.36 years, mean BMI was 27.4 ± 4.96 kg/m^2, and mean years with T2DM diagnosis was 11.1 ± 8.70 (Table 1).

Table 1 Patients characteristics.

		Frequency (percent)
Gender	Females	30 (37.0)
	Males	51 (63.0)
Marital status	Married	65 (80.2)
	Unmarried (including widowers)	16 (19.8)
Education	University education	8 (9.9)
	High school education	20 (24.7)
	Lower than high school	53 (65.4)
Treatment	Risk of hypoglycemia	63 (77.8)
	No risk of hypoglycemia	18 (22.2)
Smokers	Yes	18 (22.2)
	No	63 (77.8)
Hypertension	Yes	58 (71.6)
	No	23 (28.4)
Heart diseases	Yes	34 (42.0)
	No	47 (58.0)
Daily glycemic control	Yes	46 (56.8)
	No	35 (43.2)
	Mean	SD
Age (years)	74.2	7.36
BMI (kg/m^2)	27.4	4.96
Years with T2DM	11.1	8.7

Procedure

We invited the participants for an interview at the Diabetes Outpatients to explain them the aims of the study and to collect their written informed consent if they were interested to be enrolled. All of the enrolled patients underwent an assessment aimed to describe their socio-demographic characteristics, their lifestyles, and their cognitive efficiency (CE) or CD.

Assessment instruments

To assess their socio-demographic characteristics and their lifestyles, we used a self-report questionnaire. To assess the cognitive functions, we used the mini mental state examination (MMSE),[20,21] widely used for brief cognitive assessments (MMSE).[20,21]

The self-report questionnaire aimed to investigate which lifestyles mostly affect the health of patients with T2DM was created ad hoc after a literature review. Lifestyles considered for this study were

- dietary habits, exploring weekly consumption of bread, pasta, red meat, fish, alcohol, and daily consumption of coffee[22] and
- physical activities, exploring weekly habits of exercise (walking, aerobic activities).[23,24]

The investigated socio-demographic characteristics were: gender, age, education, marital status, and nationality. Furthermore, the questionnaire allowed us to collect information such as: body mass index (BMI), years with T2DM after first diagnosis, type of treatment. The treatment was categorized as 'drugs associated with risk of hypoglycemia' (e.g. sulfonylurea drugs) and 'drugs not associated with risk of hypoglycemia' (e.g. biguanides).

To investigate lifestyles, we used 24 Likert items exploring dietary habits and weekly physical activities. Each item was made to measure the frequency of investigated situation in a five-point scaling (1, never; 2, rarely; 3, occasionally; 4, frequently; 5, very frequently), e.g. 'In a typical week, how often do you eat red meat?' (Cronbach's $\alpha = 0.88$), 'In a typical week, how many times do you walk more than 15 minutes? (Cronbach's $\alpha = 0.82$).

The MMSE is the most widely used psychometric test to measure cognitive functions.[20] The MMSE has been well studied and validated in different populations, providing a brief and objective measure of global cognitive functioning. The test usually takes about 10 minutes to complete and can be used reliably after a short training period by physicians, nurses, and other health care professionals. The MMSE score has been found to be associated with educational level and principal lifetime occupation, and it is strongly correlated with age. For this reason, considering that is important to score the test as fairly as possible for everyone, we used the standardization of MMSE score.[25]

The overall time required for study participation was about 30 minutes.

Statistical analyses

A statistical analysis was performed using IBM Statistical Package for Social Sciences Program version 21.0 software (SPSS, Chicago, IL USA). As this was a pilot study without previous comparative data for the T2DM outpatients population, nominal variables were presented as percentage per category and compared using the Chi-squared test or Fisher's exact test, where it was appropriate. Continuous data were presented as mean and standard deviation (SD) and compared using Student's *t*-test. The correlations were described using Pearson's product moment correlation and point biserial correlation, where it was appropriate. The effects of lifestyles on changes in cognitive functions were studied using a multivariate regression model. *P*-value less than 0.05 was considered statistically significant.

Results

Considering the standardized MMSE score,[26] 59.2% ($n = 48$) had a normal score (from 25 to 30), 38.3% ($n = 31$) presented a mild CD (from 21 to 24) and 2.5% ($n = 2$) presented a moderate CD (from 10 to 20).

Table 2 The role of lifestyles in explaining cognitive functions.

Dependent variable: cognitive efficiency (*Y*)		
	Standardized β	*P*-value
Treatment (1, no risk of hypoglycemia; 2, risk of hypoglycemia)	−0.246	0.019
Weekly fish consumption	−0.059	0.362
Weekly alcohol consumption	−0.196	0.097
Weekly red meat consumption	−0.058	0.781
Weekly bread consumption	0.043	0.505
Weekly pasta consumption	−0.053	0.483
Weekly physical exercise	0.338	0.001
R^2	0.244	
Adjusted R^2	0.172	
F	3.372	0.004

There were not significantly correlations between dietary habits items and physical activities, with exception of a slight positive correlation between weekly consumption of fish and weekly consumption of bread ($r = +0.259$; *P*-value < 0.001). There was a moderate positive correlation between physical activities and MMSE score ($r = +0.397$; *P*-value < 0.001). Therefore, physical activity is positively correlated to CE. Physical activities are also in relation with the gender; hence, there was a negative correlation considering male = 1 and female = 2 ($r_{pb} = -0.279$; *P*-value < 0.05).

Patients in treatment with drugs associated with risk of hypoglycemia had less physical activities than patients treated with drugs not associated with risk of hypoglycemia; effectively, data showed a negative correlation between physical activities and treatment, considering for treatment first drugs not associated with risk of hypoglycemia (1, drugs not associated with risk of hypoglycemia; 2, drugs associated with risk of hypoglycemia; $r_{pb} = -0.291$; *P*-value < 0.001). Patients in treatment with drugs associated with risk of hypoglycemia presented more CD, considering treatment as described above and MMSE score to measure cognitive functions ($r_{pb} = -0.321$; *P*-value < 0.001). Furthermore, there was a moderate positive correlation between treatment and age ($r_{pb} = +0.278$; *P*-value < 0.05). In relation to the increase of age, there was also the presence of hypertension ($r_{pb} = +0.294$; *P*-value < 0.001). There is no correlation between MMSE standardized score and age ($P > 0.05$).

The variables exploring lifestyles – dietary habits and physical activities – were entered altogether in the same multivariable regression model to explain cognitive functions variance (*Y*; Table 2). To check model assumptions, we used residual analysis (ZRESID) and collinearity analysis, showing a residual normal distribution and no collinearity. For the role of lifestyles in explaining cognitive functions ($F = 3.372$; *P*-value = 0.004), which explained the 24% of the variance, the significant predictors were the weekly physical exercise ($\beta = +0.338$; *P*-value = 0.001) and the treatment (1, drugs not associated with risk of hypoglycemia; 2, drugs associated with risk of hypoglycemia; $\beta = -0.246$; *P*-value = 0.019). Gender, weekly fish consumption, weekly alcohol consumption, weekly red meat consumption, weekly bread consumption, and weekly pasta consumption were not predictors of CE in our regression model (*P*-value > 0.05).

Discussion

The aim of this study was to assess the relations between lifestyle and CD and to describe the prevalence of CD in outpatients over 65 years with T2DM, examining the feasibility of a future research endeavor. This study provides the basis for further investigations, considering the emerged results. In this sample, we found a prevalence of CD in T2DM outpatients treated in Policlinico San Donato, prior to this investigation, we did not have this data and it could be useful to draw future investigations, using a probabilistic sampling. The literature showed how diabetes plays a role in accelerated brain aging,[8] but understand how behaviors of T2DM patients could be in relation with cognitive functions is very important to optimize specific educational program, aimed to empower good behaviors through lifestyles. To the best of our knowledge, this study provides the first preliminary information concerning the impact of some lifestyles on cognitive functions in T2DM outpatients. Although lifestyles are considered in some non-invasive risk scores for prediction of type 2 diabetes,[27] their effects on CD is poorly studied. Growing evidence supports the concept that insulin resistance is important in the pathogenesis of CD and neurodegeneration, suggesting that brain insulin resistance is an independent risk factor for CD.[28] Moreover, the prevalence of mild CD and moderate CD in our sample – respectively 38.3% and 2.5% – are quite in line with the data presented in the literature, showing an incidence of mild CD increases to 32.7% in diabetic patients.[29] These data confirm how this issue is significant to public health, considering that CD incidence goes to 15% in adults over 65 years without diabetes.[10] Surely, the link between T2DM and CD is multifactorial, but it is not clear which predictors play a paramount role in the process of CD.[30] Moreover, lifestyles could moderate the onset of CD, and in our analysis, the physical exercise had a predictive role of CE.

The mechanisms by which physical activity improves cognition in older people are not clear. One possible mechanism is an alteration in cerebral vascular functioning and brain perfusion.[31] The benefits of physical activity, according to Lautenschlager *et al.*, were apparent after 6 months of a physical activity intervention based to encourage participants to perform at least 150 minutes of moderate–intensity physical activity per week.

Another possible mechanism is environment enrichment associated with greater physical activity.[32] Environmental enrichment is the stimulation of the brain by its physical and social surroundings, but there are no studies that describe its role as a predictor of CE in the diabetic population. Literature shows how the enriched environment contributes to enhanced brain plasticity via synaptogenesis, neurogenesis, and attenuation of neural responses to stress.[33]

Singh *et al.*[22] described how subjects following a Mediterranean diet had 33% less risk of CD, but in our study, there were not find significant associations between dietary habits and cognitive functions. This issue will be better investigated in future researches.

The importance of dietary habits and physical activities is also recently described by Zhao *et al.*[34] showing that higher intake of fish and physical exercise were associated with preventing the development of mild CD in their population-based samples. Another interesting element is given by predictor role of the drugs not associated with risk of hypoglycemia in our model. This aspect should be further investigated with more focused studies.

Limitations

Our study has a number of limitations, being a pilot study: the sample size is small, the study was conducted in one diabetes clinic, the cross-sectional data collection, the duration of the study was short, and it could be improved the measurability of lifestyles, using tools with known psychometric proprieties. Future studies should use a longitudinal design in order to identify true predictors of CE in T2DM outpatients. Another limit is given by the possible role of the treatments for the comorbidities, we have considered only the role of the drugs used for diabetic treatment. In addition, results from this study should be generalized to other countries with caution as Italian cultural aspects may have influenced dietary habits of subjects with T2DM.

Conclusion

In this study, we found that physical exercise and diet treatment were the unique predictors of CE in over 65 years outpatients with T2DM. Considering that our population will have more health problems related to aging, it is strategic understand which lifestyles could be associated with CE and mostly describe which lifestyles have a preventive role for CD.

The studies aimed to describe relations between lifestyles and cognitive functions in T2DM subjects are few, so this study has its rationale in this framework, giving some interesting data. Of course, this study provides only preliminary information to assess the feasibility of a future research endeavor.

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Disclaimer statements

Contributors RC developed the main idea. AS and MPC developed the study protocol and collected data. FP screened the citations and participated in data analysis. FD was in involved in data collection. SC and EM performed the data analysis with RC and they also reviewed the citations and the full text papers. All authors developed the final manuscript.

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Ethics approval The study was approved by Ethical Committee of Policlinico San Donato.

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