International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2025: 7.089

Association Between Type 2 Diabetes Mellitus, Cerebral Small Vessel Disease, and Cognitive Impairment: A Cross Sectional Study

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Abstract: ***Background**: Type 2 diabetes mellitus and cerebral small vessel disease are common in the elderly and are associated with cognitive impairment. **Purpose**: This study aimed to evaluate the independent and combined effects of diabetes mellitus and small vessel disease on cognitive function. **Methods**: A total of 190 participants were divided into four groups based on the presence or absence of diabetes mellitus and small vessel disease. Cognitive performance was assessed using standardized neuropsychological tests including MMSE, MOCA, memory tests, and processing speed measures. Statistical analysis was conducted at a 95% confidence level ($p < 0.05$). **Results**: Patients with both diabetes mellitus and small vessel disease demonstrated the poorest cognitive performance, particularly in global cognition, short term memory, delayed recall, attention, and processing speed. Both conditions were independently associated with cognitive impairment, while patients with either condition alone showed comparable cognitive profiles. **Conclusions**: Diabetes mellitus and small vessel disease independently contribute to cognitive impairment, supporting the hypothesis that early functional vascular dysfunction plays a role in diabetes related cognitive decline.*

Keywords: vascular cognitive impairment, cerebral microangiopathy, neuropsychological assessment, "executive function", type 2 diabetes mellitus

1. Introduction

The association between diabetes mellitus type 2 (DM) and cognitive impairments (CI) represents a significant public health issue (Kan, 2025). They frequently coexist. One of the most important diabetic complication is diabetic chronic encephalopathy, which is strongly associated with small brain vessels microangiopathy (Li, 2023). The aim of our study was to examine the associations between small vessel disease (SVD) and DM and cognitive functioning.

2. Material and Methods

We examined 38 patients with DM and SVD (61±3.86years old), 77 patients with DM without SVD (60±5.61 years old), 21 patients without DM but with SVD (62±6.83 years old) and 54 patients with no DM or SVD (61±3.87 years old). The inclusion criteria of the study were (1) age >50 years and <80 years; (2) willing to participate in the study and fulfilling of written informed consent; (3) no other neurological diseases (except SVD) such as epilepsy, stroke, brain tumor, brain trauma, demyelinating disease of the central nervous system or degenerative dementia of any kind; (4) no history of drug or alcohol abuse; (5) no severe somatic disease or infection and no decompensation of somatic disease in the last one year; (6) normal glucose level during the examination and minimum 1 week before it; (7) no history of psychiatric disease; (8) patients with DM and without DM should have similar other vascular risk factors.

After giving their informed consent and taking history data, all patients underwent somatic and neurological examination, blood test (blood count and biochemistry), urine tests, head Magnetic resonance imaging and were distributed into 4 groups: with DM and SVD, with DM without SVD, without DM and without DM and SVD. All patients were examined via the following neuropsychological battery: Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MOCA), 10 Words Memory Test (for short term memory (STM) – average from 5 trials; coefficients of fixation (Yfix), of reproduction (Yrep) and of retention (Yret), 5 min - delayed recall (DR) and recognition), 90 sec-Digit Symbol Substitution Test (DSST), Isaac Set Test (IST) for verbal fluency and Benton Visual Retention Test (BVRT).

The statistical analysis was done via descriptive analysis (for age, sex, level of education) and t-test (for normal value distribution) or non-parametric test (Mann-Witney/Wilcoxin) for analysis of association between DM and SVD and cognitive parameters via "Startgraphics 20 Plus" and SPSS 20. All results were interpreted at a 95% confidence level ($p < 0.05$)

3. Results

All groups had similar demographic characteristics (see table 1) and could be compared. Our patients had a mean age of approximately 60 years, most of them were women and with middle formal education.

Global cognitive performance. The global cognitive performance was measured by MMSE and MOCA. Patients with DM and SVD showed the poorest performance on both tests and those without SVD and DM the best ones (see table 1). Patients with DM obtained worse results than those without. SVD patients had also worse results on both tests than those without. However, there is no statistically significant difference in MMSE or MOCA results between patients with DM without SVD and those without DM but with SVD.

Verbal memory. Patients with DM and those with SVD had worse STM vs those without DM and those without SVD (see table 1). However, DM is not associated with additional STM

loss at SVD group (no statistically significant difference between DM and Non- DM groups with SVD). Moreover, patients with DM without SVD had slightly better results on STM than patients without DM but with SVD.

Patients with DM and SVD had lowest Yfix and Yrep, and those without DM and SVD had the highest ones. However, Yfix and Yrep were similar among patients with SVD with or without DM. Yrep was higher in cases with DM without SVD than in cases without DM but with SVD. Yret was similar among all patients.

The DR was similar among patients with SVD, regardless the co-existence of DM. Patients with SVD had worse DR than those without. There was no statistically significant difference in DR between patients with DM but without SVD and those without DM but with SVD.

The four groups obtained similar results for hippocampal memory (recognition).

Verbal fluency and attention. Practically we measure the categorical literal fluency of our patients via IST, which is also a measurement of cognitive processing speed. The best results had patients without DM (see table 1). However, in cases with DM, the coexistence of SVD is associated with worse verbal fluency. Besides that, among patients without DM, there was no statistically significant difference in IST performance among patients with and without SVD. Interestingly, patients with DM but without SVD had similar test result as those without DM but with SVD. Patients with DM but without SVD and those with SVD but without DM had similar verbal fluency results.

The attention was measured by DSST. The best results were obtained by patients without SVD and without DM and the worst ones by those with DM and SVD. The existence of DM and SVD were independently associated with poor performance on DSST. However, no statistically significant difference was found between the group with DM without SVD and that with SVD but without DM.

Visual memory. Visual memory was measured by BVRT (see table 1). DM and SVD were independently associated with poor BVRT performance. Among DM patients, the co-existence of SVD correlated with the number of omissions only, but not with the total number of corrects or errors. Among those without DM, SVD was associated with more errors (omissions, distortions and size errors). Interestingly, patients with DM but without SVD showed less omissions than those with SVD but without DM.

4. Discussion

DM and SVD frequently coexist among elderly patients (Li, 2023; Kan, 2025, Markus, 2025). Moreover, DM is a risk factor for the development of SVD and vascular dementia (Lyu, 2020; Kan, 2025). Besides that, not all people with DM develop SVD, although they might develop CI and even dementia of non-vascular origin (Husain, 2023). In such cases, the development of CI and dementia is suggested to be driven by other non-vascular mechanisms as direct neuronal damage, amyloid and tau accumulation, changes of neurotransmitters and some hormones (including cortisol) and direct synaptic damage (Papazafiropoulou, 2020; Husain, 2023; Lemche, 2024). However, relatively few studies have been conducted on the question of cognitive differences between patients with nonvascular and vascular DM associated CI and on the difference between non-diabetic and diabetic SVD (Zhang, 2024). Such questions are important for understanding the mechanisms of brain damage, due to DM. Our results show that the group of patients with DM and SVD had the poorest cognitive performance, as it has been obtained by other studies (Zhang, 2024). Such patients had the lowest level of global cognitive performance, STM, DR, attention, verbal fluency and BVRT, although no additional hippocampal memory dysfunction (recognition or Yret) was found among them. DM was also associated with CI even in cases without SVD. Patients with DM but without SVD had significantly lower results at MMSE, MOCA, STM, verbal fluency, attention and BVRT than those without DM and SVD. So we could support the hypothesis for additional non-vascular mechanisms of brain damage, independently associated with DM (Papazafiropoulou, 2020; Husain, 2023; Lemche, 2024). However, interesting results were obtained when to compare patients with DM without SVD and those with SVD without DM. Both groups show surprisingly similar cognitive profiles. That, along with the more pronounced CI in cases with DM and SVD vs those without DM, leads us to think that patients with DM might have some functional (not only structural) small vessel impairment, which play the key role for DM – associated CI at least at early stages. Moreover, the most impaired cognitive domains in such cases is executive function, which is associated with disconnection syndrome due to functional changes of deep white matter. The exact mechanisms of non-structural vascular brain dysfunction in cases with DM are unclear, although the role of another vascular risk factors (such as arterial hypertension, obesity, hyperglycemia, insulin resistance) has been proposed before (van Sloten, 2020; Zhang, 2024; He, 2025). This issue has practical clinical relevance because the non-structural vascular damage might be reversed if properly treated.

5. Conclusions

This study demonstrates that both type 2 diabetes mellitus and cerebral small vessel disease independently contribute to cognitive impairment, with combined presence leading to greater deficits. The findings support the role of early functional vascular dysfunction in diabetes related cognitive decline and highlight the importance of early detection and management of vascular risk factors to potentially mitigate cognitive deterioration.

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Table 1: Demographic data and statistical analysis.

	DM and SVD (1)	DM no SVD (2)	No DM, with SVD (3)	NO DM and SVD (4)	p1,2	p3,4	p1,3	p2,4	p2,3
n=	38	77	21	54					
Age (y)	61±3.86	60±5.61	61±6.83	61±3.87	>0.05	>0.05	>0.05	>0.05	>0.05
M:F	16:22	32:45	9:12	21:33					
B:M:H	3:25:10	5:52:20	1:15:5	5:40:9					
MMSE (p.)	25.34±2.37	27.06±2.0	27.29±1.27	28.19±1.68	**0.0010**	**0.0382**	**0.0167**	**0.0013**	>0.05
MOCA (p).	23.5±3.21	26.03±1.88	26.61±1.37	28.09±2.06	**0.0002**	**0.0025**	**0.0023**	**0.0069**	>0.05
STM	5.33±1.68 Med 5.0	6.24±1.04 Med 6.2	5.45±0.25 Med 5.4	Med 5.8	**0.0006**	**0.0063**	>0.05	**0.0003**	**0.0482**
Yfix	53.32±16.81	62.36±10.49	62±14.24	68.67±11.95	**0.0006**	**0.0435**	>0.05	**0.0018**	>0.05
Yrep	71.43±32.44 Med71.32	Med 75.0	71.43±14.74	78.23±13.14 Med77.7778	>0.05	**0.0144**	>0.05	**0.0265**	>0.05
Yret	77.93±38.81 Med 87.5	Med 88.2353	86.59±17.53 Med 87.1	90.23±14.62 Med89.7436	>0.05	>0.05	>0.05	>0.05	>0.05
DR (p.)	4.37±2.60	5.38±1.48	5.38±1.63	6.19±1.43	**0.0093**	**0.0367**	>0.05	**0.0022**	>0.05
Recogn	18.32±2.3	18.21±5.6	18.32±3.92	18.48±3.6	>0.05	>0.05	>0.05	>0.05	>0.05
DSST т	Med 21.0	29.53±11.23 Med 29.0	27.24±8.48 Med 29.0	37.28±11.73	**0.0109**	**0.0006**	0.0001	**0.0002**	>0.05
IST (p.)	28.16±6.88 Med 28.5	Med 32.0	32.48±3.87	34.20±4.15 Med 32.0	**0.0042**	>0.05	**0.0105**	**0.0032**	>0.05
BVRT COR	3.14±1.94	3.66±1.63	3.85±1.31	4.94±1.55	>0.05	**0.0064**	>0.05	**0.0001**	>0.05
BVRT ER	11.97±5.40	10.69±4.00	10.00±2.77	6.70±2.78	>0.05	**0.0001**	0.05	**0.0001**	>0.05
BVRT om	Med 2,0	Med 1.0	Med 2.0	Med 1.0	**0.0133**	**0.0060**	>0.05	**0.0181**	**0.0421**
BVRT dys	4.26±2.94	3.95±2.09 Med 4.0	3.35±1.66 Med 3.0	Med 2.0	>0.05	**0.0033**	>0.05	**0.0001**	>0.05
BVRT per	Med 1.0	Med 1.0	Med 1.0	Med 1.0	>0.05	>0.05	>0.05	>0.05	>0.05
BVRT rot	1.97±1.42	1.95±1.30	1.55±1.15	1.93±1.01	>0.05	>0.05	>0.05	>0.05	>0.05
BVRT mis	Med 1.0	1.45±1.12 Med 1.0	Med 1.0	0.77±0.69 Med1.0	>0.05	>0.05	>0.05	**0.0002**	>0.05
BVRT size	Med 1.0	Med 1.0	Med 1.0	Med 0.0	>0.05	**0.0288**	>0.05	**0.0437**	>0.05

Legend: DM – diabetes mellitus, SVD – small vessel disease; M:F – male:female ratio; B:M:H – patients with basic, with middle and with high formal education; MMSE – Mini Mental State Examination; MOCA - Montreal Cognitive Assessment; STM – short term memory (average result from 5 trials of immediate recall), DR – 5 min delayed recall; Yfix,ret, rep – coefficients of fixation, retention and reproduction (10 words test); Recogn – recognition (number of words from list of 20 words), IST – Isaac Set Test, BVRT – Benton Visual Retention Test COR – number of corrects; ER – number of Errors, om – omissions, dys – distortions, per – perseverations, rot – rotations, mis – misplacements, size – size – errors.

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