European Journal of Clinical Pharmacy
Print ISSN: 2385-409X **Online ISSN**: Applied Website:
https://farmclin.com/

Early Microvascular Dysfunction and Its Association with Cognitive and Vascular Risk Profiles

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ABSTRACT

Background:
Early microvascular dysfunction is an important marker of vascular disease and may contribute to cognitive decline. Endothelial injury can affect blood flow to the brain and may worsen cognitive performance. Limited local data are available regarding the relationship between endothelial dysfunction and vascular risk factors.

Objective:
To assess the association of early microvascular dysfunction with cognitive function and vascular risk profiles among adult participants.

Methods:
This cross-sectional observational study was conducted at Zhujiang Hospital of Southern Medical University from July 2025 to December 2025. A total of 240 participants aged 30–70 years were enrolled through consecutive sampling. Endothelial function was assessed by brachial artery flow-mediated dilatation. Cognitive status was evaluated using the Montreal Cognitive Assessment score. Demographic, clinical, and laboratory data including hypertension, diabetes mellitus, smoking, obesity, and lipid profile were recorded. Statistical analysis was performed using IBM SPSS Statistics.

Results:
The mean age of participants was 52.8 ± 10.6 years. Early microvascular dysfunction was present in 98 (40.8%) participants. Mean MoCA score was significantly lower in participants with endothelial dysfunction compared to those without dysfunction (20.9 ± 3.2 vs 25.1 ± 3.1, $p<0.001$). Flow-mediated dilatation showed significant positive correlation with MoCA score ($r=0.521$, $p<0.001$). Hypertension, diabetes mellitus, smoking, obesity, and elevated LDL cholesterol were significantly associated with impaired endothelial function. Regression analysis showed that reduced flow-mediated dilatation independently predicted lower cognitive scores.

Conclusion:
Early microvascular dysfunction is strongly associated with cognitive impairment and vascular risk factors. Early identification of endothelial dysfunction may help reduce future vascular and cognitive complications.

KEYWORDS: Microvascular dysfunction; Cognitive impairment; Endothelial dysfunction; Vascular risk factors; Flow-mediated dilatation.

How to Cite: Husnain Abbas, Khawar Shahzad, Athar Parvaiz, Saad Siddiqui, Rafaqat Malik, Li Zhou, (2025) Early Microvascular Dysfunction and Its Association with Cognitive and Vascular Risk Profiles, European Journal of Clinical Pharmacy, Vol.7, No.1, pp. 9069-9073.

INTRODUCTION

Cardiovascular and cerebrovascular diseases are major health problems worldwide [1]. Many vascular changes start silently before the appearance of major clinical symptoms. Early microvascular dysfunction is considered one of the earliest signs of endothelial injury and vascular disease [2]. It affects the normal function of blood vessels and may reduce blood supply to important organs including the brain [3]. Recent evidence suggests that endothelial dysfunction may also contribute to early cognitive decline and poor neurological outcomes [4].

The vascular endothelium plays an important role in maintaining vascular tone, blood flow, inflammation control, and nitric oxide production [5]. When endothelial function becomes impaired, blood vessels lose their normal ability to dilate properly. This leads to complication such as, vascular stiffness, inflammation, oxidative stress, and reduced tissue perfusion [6]. It gradually damages cerebral circulation affecting the cognitive functions. Chronic hyperglycemia and high blood pressure can

directly impair blood vessel walls causing the microvascular damage[7, 8].

Cognitive impairment has become an important public health concern due to increasing life expectancy and rising burden of vascular disease [9]. Early identification of patients at risk is necessary because mild cognitive changes may progress to severe cognitive decline if not recognized on time [10]. Previous studies have shown that endothelial dysfunction may be associated with reduced cognitive performance even before the development of stroke or dementia [8]. However, the relationship between early microvascular dysfunction and cognitive profile remains insufficiently explored in many populations.

Flow-mediated dilatation is a simple, non-invasive, and widely accepted method for assessing endothelial function. It reflects vascular responsiveness and endothelial health. The Montreal Cognitive Assessment is also a practical screening tool for early cognitive impairment [11]. Evaluation of these parameters together may help identify individuals at high vascular and neurological risk.

Despite growing international evidence, limited data are available regarding the association of endothelial dysfunction with cognitive status and vascular risk profiles in clinical populations. Understanding this relationship may help improve early prevention strategies and vascular risk management. Therefore, the present study was conducted to assess the association between early microvascular dysfunction, cognitive function, and vascular risk factors among adult participants presenting to a tertiary care hospital in China..

METHODOLOGY

This observational cross-sectional study was conducted at Zhujiang Hospital of Southern Medical University over a period of six months from July 2025 to December 2025. The study was reported according to the STROBE guidelines for observational studies. Adult participants attending the neurology and internal medicine outpatient departments were enrolled to evaluate early microvascular dysfunction and its association with cognitive and vascular risk profiles. A total sample size of 240 participants was calculated using OpenEpi version 3.01 by taking a 95% confidence level, 5% margin of error, anticipated prevalence of microvascular dysfunction of 20%, and 10% allowance for incomplete data. Non-probability consecutive sampling was used.

Participants aged 30 to 70 years of either gender were included. Patients with previous stroke, diagnosed dementia, severe psychiatric illness, chronic inflammatory disease, malignancy, severe renal or hepatic failure, active infection, pregnancy, or inability to complete cognitive testing were excluded. Individuals using medications known to markedly affect vascular tone, such as long-term vasodilator therapy, were also excluded to reduce confounding. Potential confounders including age, gender, smoking status, diabetes mellitus, hypertension, obesity, dyslipidemia, and physical inactivity were recorded and adjusted during analysis.

After written informed consent, demographic and clinical data were collected using a structured proforma. Blood pressure was measured using a standard calibrated digital sphygmomanometer after five minutes of rest. Body mass index, fasting blood glucose and lipid profile were assessed from venous blood samples processed in the hospital laboratory. Early microvascular dysfunction was assessed by brachial artery flow-mediated dilatation using high-resolution vascular ultrasound performed by a trained radiologist under standardized conditions. Cognitive function was evaluated using the Montreal Cognitive Assessment (MoCA) tool [11].

Data were entered and analyzed using IBM SPSS-26 software. Continuous variables were presented as mean ± standard deviation, while categorical variables were expressed as frequency and percentage. Independent sample t-test and chi-square test were used for comparison where appropriate. Pearson or Spearman correlation analysis was applied to assess the relationship between microvascular dysfunction and cognitive scores. Multivariable linear regression analysis was performed to control for confounders. Missing data of less than 5% were handled by complete case analysis. A p-value of less than 0.05 was considered statistically significant.

Ethical approval was obtained from the Institutional Ethics Committee of Zhujiang Hospital of Southern Medical University under reference number ZJH-SMU-2025-071.

RESULTS

A total of 240 participants were included in the final analysis. The mean age of the participants was 52.8 ± 10.6 years. Among them, 136 (56.7%) were males and 104 (43.3%) were females. Early microvascular dysfunction was identified in 98 (40.8%) participants based on impaired flow-mediated dilatation values. Baseline demographic and clinical characteristics of the study population are shown in Table 1.

Table 1: Baseline demographic and clinical characteristics of study participants (n=240)

Variables	Frequency (%) / Mean ± SD
Age (years)	52.8 ± 10.6
Male gender	136 (56.7%)
Female gender	104 (43.3%)
Body mass index (kg/m²)	27.1 ± 4.3

Variables	Frequency (%) / Mean ± SD
Current smokers	74 (30.8%)
Hypertension	112 (46.7%)
Diabetes mellitus	88 (36.7%)
Dyslipidemia	96 (40.0%)
Physically inactive participants	118 (49.2%)
Systolic blood pressure (mmHg)	136.4 ± 18.7
Diastolic blood pressure (mmHg)	84.2 ± 10.1
Fasting blood glucose (mg/dL)	118.6 ± 32.4
Total cholesterol (mg/dL)	201.8 ± 39.7
LDL cholesterol (mg/dL)	126.3 ± 31.5
HDL cholesterol (mg/dL)	42.6 ± 8.4
Triglycerides (mg/dL)	171.2 ± 48.6
Flow-mediated dilatation (%)	6.8 ± 2.1
MoCA score	23.4 ± 3.8

Participants with microvascular dysfunction had significantly lower MoCA scores and higher vascular risk burden compared to participants without dysfunction. Comparative analysis between both groups is shown in Table 2.

Table 2: Comparison between participants with and without early microvascular dysfunction

Variables	Microvascular Dysfunction Present (n=98)	No Dysfunction (n=142)	p-value
Age (years)	56.2 ± 9.4	50.4 ± 10.8	<0.001
Male gender, n (%)	61 (62.2%)	75 (52.8%)	0.148
Body mass index (kg/m²)	28.5 ± 4.6	26.1 ± 3.8	<0.001
Hypertension, n (%)	63 (64.3%)	49 (34.5%)	<0.001
Diabetes mellitus, n (%)	48 (49.0%)	40 (28.2%)	0.001
Current smokers, n (%)	39 (39.8%)	35 (24.6%)	0.012
Total cholesterol (mg/dL)	214.6 ± 36.8	192.9 ± 38.7	<0.001
LDL cholesterol (mg/dL)	136.8 ± 29.6	119.1 ± 30.5	<0.001
Flow-mediated dilatation (%)	4.9 ± 1.1	8.1 ± 1.5	<0.001
MoCA score	20.9 ± 3.2	25.1 ± 3.1	<0.001

Correlation analysis demonstrated a significant positive association between flow-mediated dilatation and cognitive performance. Higher vascular risk parameters were negatively associated with endothelial function and cognitive scores. Correlation coefficients are presented in Table 3.

Table 3: Correlation of flow-mediated dilatation with cognitive and vascular risk parameters

Variables	Correlation coefficient (r)	p-value
MoCA score	0.521	<0.001
Age	-0.402	<0.001
Body mass index	-0.318	<0.001
Systolic blood pressure	-0.447	<0.001
Fasting blood glucose	-0.369	<0.001
LDL cholesterol	-0.341	<0.001
Triglycerides	-0.286	<0.001

Multivariable linear regression analysis showed that lower flow-mediated dilatation remained independently associated with lower MoCA scores after adjustment for age, gender, diabetes mellitus, hypertension, smoking, and lipid profile. Age and hypertension also showed independent significant associations with cognitive performance as shown in Table 4.

Table 4: Multivariable linear regression analysis for predictors of lower MoCA score

Variables	Beta coefficient (β)	Standard Error	p-value
Flow-mediated dilatation (%)	0.428	0.061	<0.001
Age (years)	-0.291	0.034	<0.001
Hypertension	-0.188	0.742	0.003
Diabetes mellitus	-0.121	0.694	0.041

Variables	Beta coefficient (β)	Standard Error	p-value
Smoking status	-0.084	0.653	0.118
LDL cholesterol	-0.097	0.011	0.072
Male gender	0.052	0.587	0.331

DISCUSSION

The present study showed a significant association between early microvascular dysfunction, cognitive decline, and vascular risk factors. Early vascular changes are now considered an important pathway in the development of cognitive impairment and future cardiovascular disease [12]. Our findings support the idea that endothelial dysfunction may appear before major clinical complications and may affect both vascular and brain health at the same time.

In our study, participants with impaired flow-mediated dilatation had significantly lower MoCA scores. This finding suggests that reduced endothelial function is linked with poor cognitive performance. The endothelium plays an important role in maintaining cerebral blood flow and oxygen delivery to brain tissue. When endothelial function becomes impaired, nitric oxide production decreases, vascular inflammation increases, and cerebral perfusion may become reduced [6]. These changes can gradually affect memory and attention. Previously published literature also reports that endothelial dysfunction is linked with poor cognitive performance [13-15].

Hypertension and diabetes mellitus and increased age showed a strong negative association with endothelial function and cognitive score in our results. Oxidative stress, inflammation and reduced vascular elasticity linked with these conditions may damage small blood vessels and reduce blood supply to the brain [16]. Persistent high blood pressure causes mechanical stress on vessel walls, while hyperglycemia leads to endothelial injury and microvascular damage. This may explain the lower flow-mediated dilatation values observed in these patients. Previous literature has also shown that diabetes and hypertension are major contributors to endothelial dysfunction and vascular cognitive changes [17].

Obesity, dyslipidemia, and smoking also showed significant association with endothelial dysfunction in our study. Increased body mass index and abnormal lipid profile promote chronic low-grade inflammation and vascular injury [18]. Elevated LDL cholesterol contributes to atherosclerotic changes and reduces vascular compliance. Smoking further worsens endothelial health by increasing oxidative stress and reducing nitric oxide bioavailability [19]. These mechanisms may collectively impair vascular reactivity and cerebral circulation. A recent meta-analysis also confirmed reduced flow-mediated dilatation among smokers [20].

The positive correlation between flow-mediated dilatation and cognitive score in our study highlights the importance of vascular health in maintaining normal brain function. Participants with better endothelial function had better cognitive performance. This relationship remained significant even after adjustment for confounding factors in regression analysis. This indicates that endothelial dysfunction may independently contribute to early cognitive impairment rather than simply reflecting the effect of age or comorbid disease[12].

The clinical importance of this study is that early endothelial dysfunction may serve as a simple non-invasive marker for identifying individuals at risk of future cognitive decline and vascular disease. Flow-mediated dilatation assessment can help in early risk stratification before irreversible complications develop. Early control of hypertension, diabetes, obesity, smoking, and dyslipidemia may improve vascular health and possibly reduce cognitive decline.

This study has some limitations. It was a single-center cross-sectional study, so causal relationship could not be confirmed. The sample size was moderate and long-term follow-up was not performed. Advanced neuroimaging and inflammatory biomarkers were also not included. Future multicenter prospective studies with larger populations and long-term follow-up are needed to further explore the relationship between endothelial dysfunction and cognitive decline.

CONCLUSION

Early microvascular dysfunction showed a strong association with cognitive impairment and vascular risk factors in our study population. Reduced flow-mediated dilatation was independently linked with lower cognitive performance. Vascular risk factors such as hypertension, diabetes, obesity, smoking, and dyslipidemia were strongly associated with endothelial dysfunction. Early identification and management of vascular dysfunction may help reduce future cognitive and cardiovascular complications.

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