



MICRO LABS LIMITED

# Diabetes Update

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Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you **"DIABETES UPDATE"** which contains latest and interesting news in the field of Diabetes and Endocrinology.

- Sedentary time with carotid atherosclerotic plaques in type 2 diabetes patients
- Diabetic myonecrosis: Diagnosis and Management Challenges
- Diabetes duration and weight loss are associated with onset age and remote metastasis of pancreatic cancer in patients with diabetes mellitus
- Using the magnitude of low-frequency fluctuation to study altered spontaneous brain activity patterns in diabetic retinopathy patients.

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## Sedentary time with carotid atherosclerotic plaques in type 2 diabetes patients

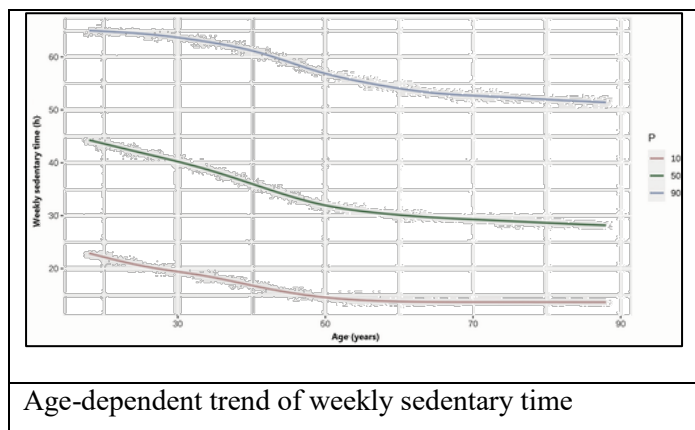
In diabetic individuals, cardiovascular disease (CVD), which includes coronary artery disease (CAD), stroke, and peripheral artery disease (PAD), is a well-known main cause of death. One of the key underlying reasons is atherosclerosis. Despite the fact that metabolic problem in diabetes has been proven to be a key mediator in the initiation and progression of atherosclerosis, there are still some potential associated molecules that could influence the progression of atherosclerosis in diabetes.<sup>1</sup> Atherosclerosis, the fundamental degenerative process in most cardiovascular disorders, can start early in childhood and go unnoticed for a long time before developing to its later stages. The peripheral and carotid arteries have been the primary targets for early diagnosis of atherosclerosis in otherwise healthy people.<sup>2</sup>

Using national multicenter data, this study looked at the association between weekly sedentary time (WST) and other lifestyle behaviours and carotid atherosclerotic plaques in T2DM patients.<sup>3</sup>

From June 2017 to April 2021, a total of 26 664 subjects with T2DM were enrolled from 10 National Metabolic Management Centers (MMCs). WST, sleeping time, smoking and drinking information, carotid artery ultrasonography, and biochemical parameters were all acquired from self-reported lifestyle data. Using multivariable logistic regression models, the independent association of carotid plaque with sedentary and other lifestyle habits was assessed, and odds ratios (OR) with 95 percent confidence intervals (CI) were reported. Furthermore, stratified analysis was used to show the impact of confounding factors.

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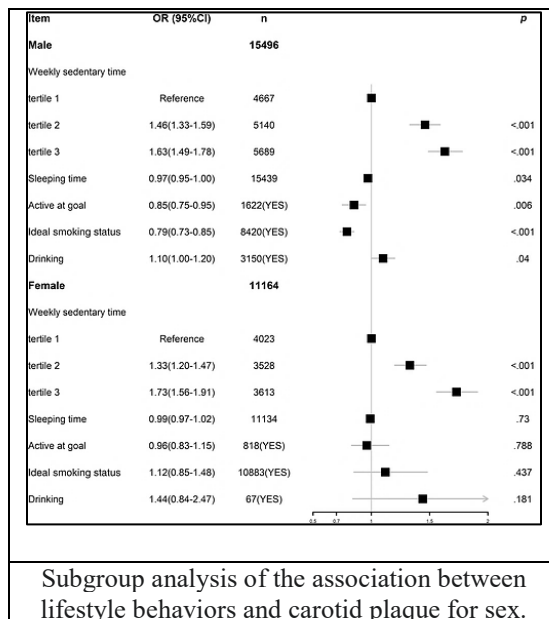
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The individuals' median (interquartile range) weekly sedentary time (WST) was 35.0 (21.0, 42.0) h, with a mean (SD) age of 54.0 (11.6) years. Participants in the second and third tertiles of the WST were younger and had diabetes for a shorter period of time than those in the first tertile. After correction, there were positive relationships between prolonged sedentary time and the odds of arterial plaque, with corresponding ORs of 1.40 (95 percent CI: 1.31–1.50) and 1.67 (95 percent CI: 1.56–1.79) in the second and third tertiles, respectively. However, there was no statistical significance in the effect of WST on plaque in patients aged 18–40 years old; the p value in the third tertile was 0.163.

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A study by Muray P et al, higher physical activity and less sedentary time were linked to a decreased prevalence of intraplaque bleeding in 90 asymptomatic patients.<sup>4</sup> Reduced sedentary activities in clinical settings could enhance cardiometabolic risk factors like waist circumference, fat percentage, and glycemic management, according to a meta-analysis. Furthermore, differences in age were linked to varied degrees of sedentary time in this study. Surprisingly and intriguingly, the data revealed that older persons spend the least amount of time inactive than other age groups, contradicting our expectations and findings from other nations. This research suggests that sedentary time may have a negative impact on the establishment and progression of carotid plaque via metabolic markers, but more research is needed to determine the exact mechanism.<sup>3</sup>

Higher weekly sedentary time appears to be linked to a higher prevalence of carotid plaque in T2DM patients, particularly in the elderly.

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## Diabetic myonecrosis: Diagnosis and Management Challenges

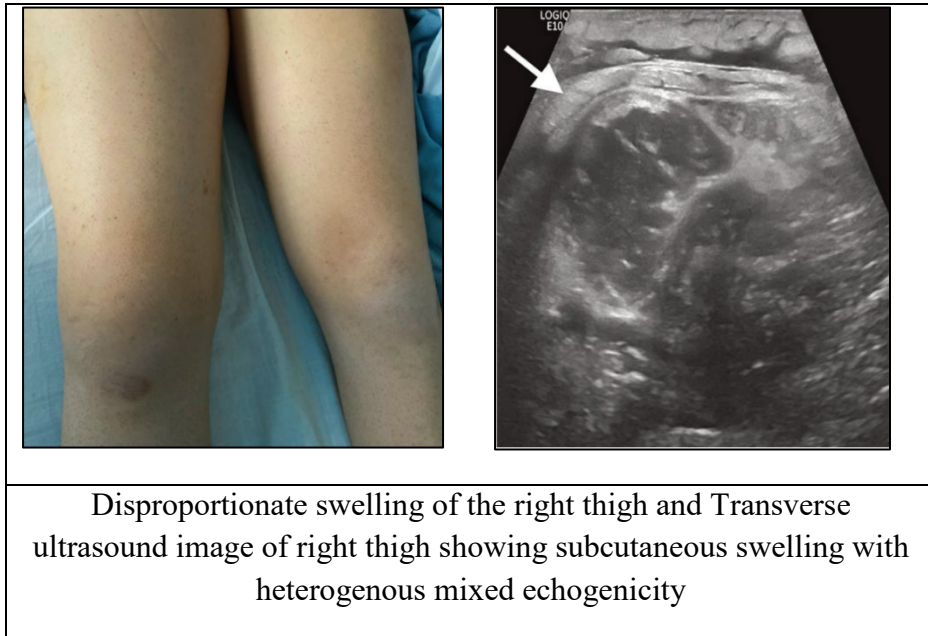
Diabetic myonecrosis (DMN) is an uncommon consequence of poorly treated long-term diabetes that is mostly unknown. Acute onset muscular soreness and high inflammatory markers are common symptoms, and the condition might be mistaken for infection or autoimmune-mediated myopathy.<sup>1</sup> Its cause is unknown, however it is considered to be due to microvascular occlusion, which causes skeletal muscle necrosis. It usually affects the proximal muscles of the lower legs, but it can also affect the bilateral or distal muscle groups. Other diabetes-related problems, such as retinopathy, nephropathy, and neuropathy, are common in patients who acquire myonecrosis.<sup>2</sup> This study examines a case of DMN, the multidisciplinary strategy used, and the problems encountered in the patient's care.

## Case Presentation:

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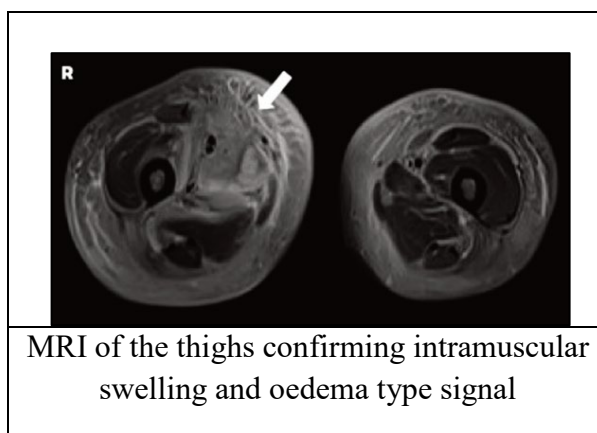
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24 hours after peritoneal dialysis catheter insertion, a 31-year-old woman presented with acute right thigh pain and swelling. She had type 1 diabetes mellitus for more than 20 years prior to her presentation. Her glycemic control had been poor, with repeated episodes of diabetic ketoacidosis and consequences such as diabetic retinopathy, gastroparesis, autonomic neuropathy, and end-stage renal disease due to diabetic nephropathy, which necessitated peritoneal dialysis. She was discharged after finishing an IV antibiotic course for a suspected infection, but she returned to her renal team one week later with increased right thigh pain and swelling. She was in excruciating discomfort during the test. Her pulse rate was 110 beats per minute, and her blood pressure was 158/90 mmHg.



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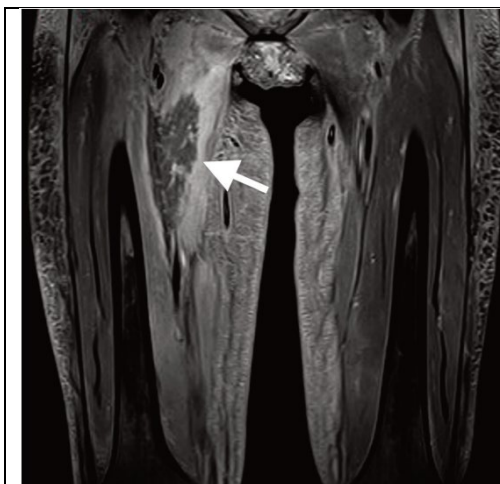
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The presence of unilateral substantial right medial compartment muscle edoema, myositis, and ischaemia was verified by magnetic resonance imaging (MRI) of both thighs. The sartorius, adductor longus, and vastus intermedius were the most affected. There was no marrow infarction, osteomyelitis, or focal soft tissue or osseous collection. The patient was given intravenous antibiotics for possible infective reasons such as pyomyositis at the time of presentation. Despite a lengthy course of broad-spectrum intravenous antibiotics, symptomatic improvement was minimal. A diagnosis of DMN was made based on a long history of poorly controlled diabetes with microvascular complications, as well as the clinical presentation and radiological findings. Throughout her stay, the diabetes specialty nurse and diabetologist provided ongoing advice, suggesting rigorous glycemic control, analgesics, and bedrest.

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Intense muscle, fascial and subcutaneous enhancement within the right upper medial thigh with focal central area of muscular non-enhancement

Any diabetic patient with spontaneous painful swelling of the limbs should have myonecrosis high on the differential diagnosis list. The final diagnosis of non-infectious myonecrosis can be difficult, and many patients require repeated tests to rule out other possibilities. One of the most frequently accepted underlying diseases for ischemic myonecrosis is arteriosclerosis obliterans.<sup>4</sup> The afflicted muscle area shows classic iso- to hypointensity on T1-weighted imaging and high signal intensity on T2-weighted imaging, as well as concomitant subcutaneous fat oedema. Muscle biopsy is not commonly used to support the diagnosis of DMN because of the increased time to symptomatic improvement and procedure-related complications. Histology is often reserved for cases with unusual clinical signs and symptoms. When compared to surgical intervention such as excision of infarcted muscle, nonsurgical management shows a statistically significant improvement in time to recovery.<sup>3</sup>

Early involvement of the diabetes team at the time of admission is crucial in the management of patients with confirmed or suspected diabetic myonecrosis. A multidisciplinary approach to the diagnosis and management of diabetic myonecrosis is essential

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## Diabetes duration and weight loss are associated with onset age and remote metastasis of pancreatic cancer in patients with diabetes mellitus

Diabetes and cancer are frequent diseases that have a huge impact on people's health all around the world. Diabetes has been linked to an increased risk of several of the more common malignancies, but data on many others, particularly the less common cancers, is limited or nonexistent, necessitating more research. Even more uncertainty exists when it comes to diabetes and cancer prognosis or cancer-specific mortality. It's still uncertain whether there's a direct link between diabetes and cancer (eg, due to hyperglycemia).<sup>1</sup> Diabetes mellitus has been linked to pancreatic cancer in prior epidemiological research, with diabetes patients having a twofold increased chance of getting pancreatic cancer. It has been discovered that among pancreatic cancer patients receiving pancreaticoduodenectomy, over half of those with recent-onset diabetes had their diabetes resolve paradoxically postoperatively, but those with long-standing diabetes have no effect.<sup>2</sup> Many cancers have weight loss as one of their clinical symptoms, and extreme weight loss might show as cachexia. The amount of weight lost often reflects the tumor's aggressiveness and rate of advancement. Newly diagnosed type 2 diabetes mellitus (T2DM) is commonly associated by weight gain, according to studies. Pancreatic

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cancer (PC)-associated newly diagnosed DM, on the other hand, is frequently accompanied by weight loss prior to the diagnosis of PC.<sup>3</sup>

The aim of this study was to look at the clinical characteristics of individuals with pancreatic cancer (PC) and diabetes, as well as the impact of diabetes duration and weight loss on PC tumour biological behaviour.

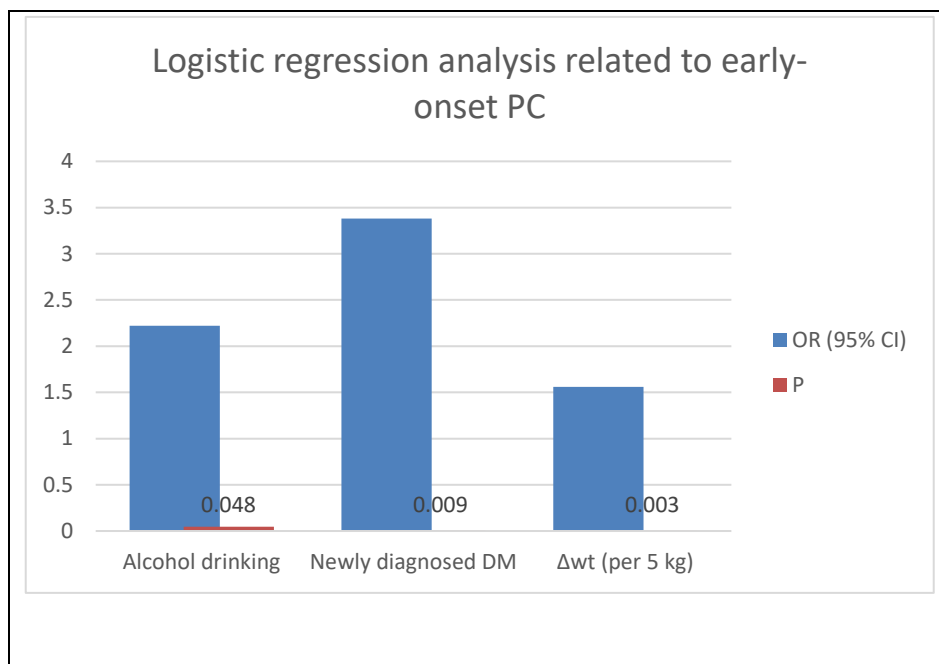
In patients with PC and DM, a retrospective analysis was done. The data was gathered by searching both electronic and paper medical records. Tumor size, metastasis, tumor/node/metastasis (TNM) staging, surgical procedures, and other factors were all considered. The size of the tumour was determined using an enhanced computed tomography scan of the abdomen or observations from the surgery data. PC was characterised as having an onset age of less than 50 years old. The onset age of PC was deemed equivalent to the diagnosis age due to the rapid progression and brief medical history of PC. As a result, patients were divided into two groups based on the age of onset of PC: early-onset PC (onset age less than 50 years old) and late-onset PC (onset age greater than 50 years old) (onset age more than 50 years old). Diabetic duration of less than two years was defined as new-onset DM, whereas diabetic duration of more than two years was characterised as long-standing DM. Patients were divided into two groups based on the entire population's median weight loss (5 kg): the heavy weight loss group ( $\Delta Wt \geq 5$  kg) and the control group ( $\Delta Wt < 5$  kg) with slight or no weight loss. The connection between diabetes duration, weight loss, and early-onset PC, distant metastasis was investigated using logistic regression analysis.

Patients with early-onset PC had a greater proportion of new-onset DM (35 [79.5 percent] vs. 217 [46.9%],  $p < 0.001$ ), were smokers and drinkers, and had more noticeable weight loss (8.5 [3.8, 15] kg vs. 5 [0, 10] kg,  $p < 0.001$ ). Patients with distant metastases were younger at diagnosis, lost more weight, had a lower BMI, and were more likely to smoke, but their cancer was less likely to be confined in the head of the pancreas. New-onset

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diabetes and weight loss were found to be independently linked to early-onset PC in regression analysis: odds ratio (OR) = 3.38 (95 percent CI 1.36-8.4,  $p = 0.09$ ; OR = 1.56 (95 percent CI 1.16-2.1),  $p = 0.003$ , respectively. Long-term diabetes and severe weight loss, on the other hand, were found to be independently linked to remote metastasis: OR = 3.38 (95 percent CI 1.36-8.4,  $p = 0.09$ ; OR = 1.56 (95 percent CI 1.16-2.1),  $p = 0.003$ , respectively.



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| Independent factors                                       | OR (95% CI)      | p      |
|-----------------------------------------------------------|------------------|--------|
| BMI                                                       | 0.83 (0.73–0.94) | 0.005  |
| Smoking                                                   | 2.01 (1.01–4.25) | 0.046  |
| Long-term DM                                              | 3.42 (1.53–7.67) | 0.003  |
| Heavy weight loss ( $\Delta Wt \geq 5$ kg)                | 2.21 (1.02–4.79) | 0.044  |
| Position of tumor (head)                                  | 0.26 (0.12–0.54) | <0.001 |
| Logistic regression analysis related to remote metastasis |                  |        |

A pooled study indicated that DM lasting more than two years significantly increased the risk of PC (odds ratio [OR] = 1.9, 95 percent confidence interval [CI] 1.72–2.09), even when the duration of DM was prolonged to 20 years (OR = 1.3, 95 percent confidence interval [CI] 1.03–1.63).<sup>4</sup> In patients with new-onset DM, a high-risk population for PC, several researchers have proposed a PC risk prediction model. PC risk can be assessed and forecasted using the patient's age, BMI, BMI change, smoking, medication, and other biochemical indicators.<sup>5</sup> In this study, patients who lost a lot of weight were diagnosed with PC earlier and had more new-onset diabetes than the control group. As previously stated, new-onset DM with significant weight loss is an essential clinical indicator to look for before a PC diagnosis. Patients with apparent weight loss had a higher proportion of advanced PC with distant metastases, according to this study. Heavy weight loss was found to be an independent risk factor for distant metastases and reduced radical surgery in a logistic regression study. As a result, weight loss is not only a first clinical symptom that aids in the early discovery and diagnosis of PC, but it is also a reflection of extremely malignant biological behaviour that indicates poor PC survival and prognosis.<sup>3</sup>

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Early-onset PC was frequently manifested by new-onset diabetes and weight loss, which necessitated additional attention. Long-term diabetes and extreme weight loss were found to be risk factors for distant metastases, indicating that these characteristics may play a role in patients with PC having a poor prognosis.

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**Using the magnitude of low-frequency fluctuation to study altered spontaneous brain activity patterns in diabetic retinopathy patients.**

Diabetic retinopathy (DR), the most prevalent consequence of diabetes mellitus, is causing an escalating burden of preventable vision loss that is threatening to overwhelm worldwide eye-care facilities.<sup>1</sup> Retinal injury

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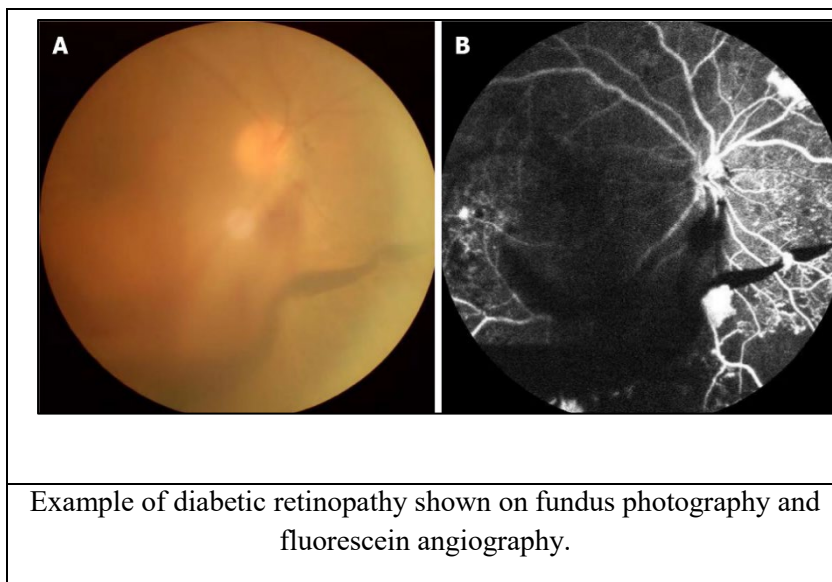
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induces neovascular development in peripheral diabetic retinopathy (PDR). The retina is harmed by neovascular development, which can lead to fibrosis and even retinal detachment. The vitreous can potentially become neovascularized, resulting in vitreous haemorrhage. There has recently been further evidence that diabetics' brains have similar microvascular damage. The brains of patients with chronic diabetes had significant microvascular and neurological damage, according to autopsy findings.<sup>2</sup> The association between diabetic retinopathy and altered brain function connections is unknown. Using the amplitude of low-frequency fluctuation (ALFF) approach, this study attempted to evaluate the association between this brain activity and clinical signs and behaviours of DR patients.

A total of 24 DR patients and 24 healthy controls (HC) were chosen at random for this investigation. The patients underwent MRI scans with 3-Tesla MRI scanners. Based on the rs-fMRI data analysis toolkit, Data Processing Assistant for the advanced edition of Resting-State fMRI software was used for digital imaging communications in medicine (DICM) form conversion, head motion correction, slice timing, realignment, spatial normalisation, full width smoothing with a Gaussian kernel of  $6\text{ mm} \times 6\text{ mm} \times 6\text{ mm}$  at half-maximum, detrending, and nuisance covariates regression. After adjustment for head motion, the fMRI images were unified to the Montreal Neurological Institute spatial standard using a conventional echoplanar imaging template, and the images were resampled to a resolution of  $3\text{ mm} \times 3\text{ mm} \times 3\text{ mm}$ . The ALFF of each voxel was divided by the average whole-brain ALFF value for each subject to diminish the effect of participant variety. REST software was used to separate different brain areas of these groups into areas of interest based on the ALFF data. The average ALFF values of numerous brain areas in the DR group were compared to clinical data ( $P < 0.05$ ).

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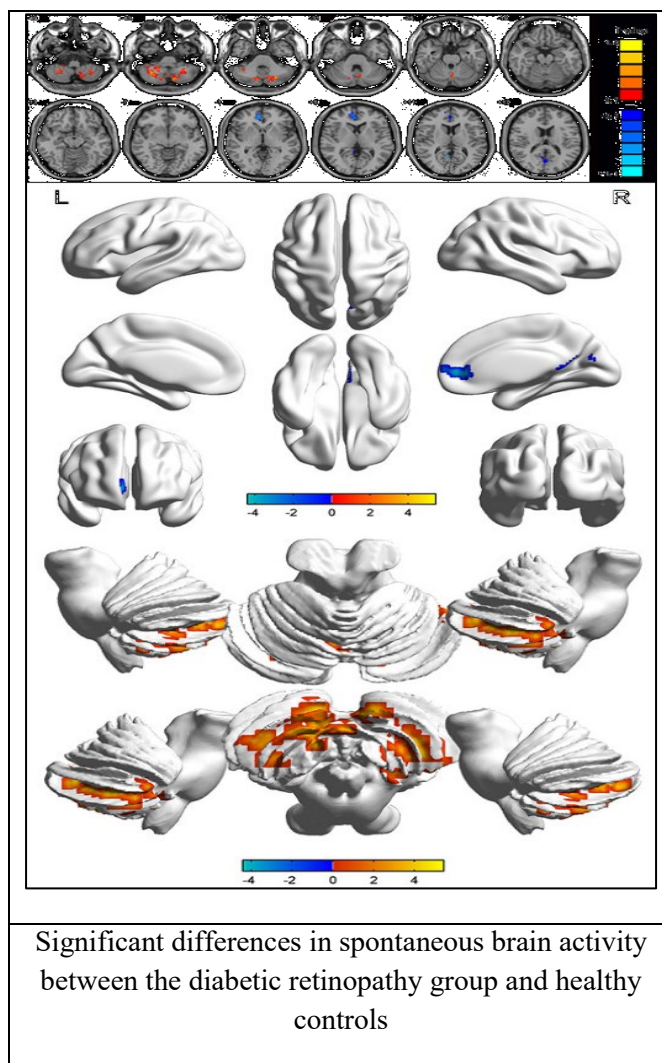
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The ALFF values of the left and right posterior cerebellar lobes, as well as the right anterior cingulate gyrus, were significantly greater in the DR patients than in the HCs; however, the ALFF values of the bilateral calcarine area were significantly lower in the DR patients. The area under the curve study of receiver operating characteristic (ROC) curves of different brain areas revealed high accuracy. There was no correlation between mean ALFF values for various locations and clinical manifestations in DR patients. Anomalies in neuronal synchronisation in several brain regions of DR patients have been linked to cognitive and visual problems.

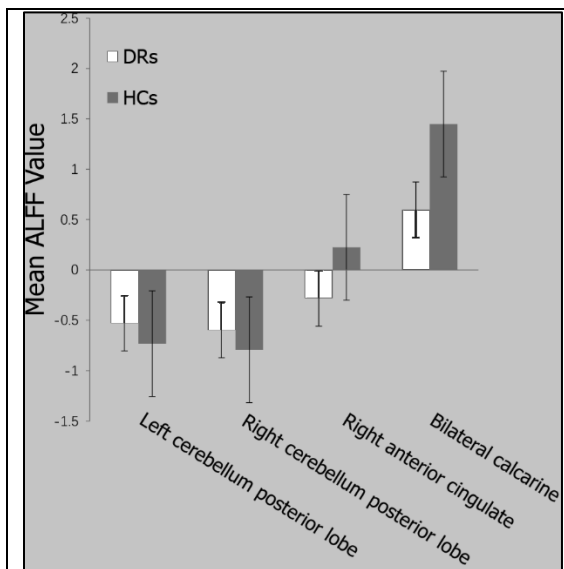
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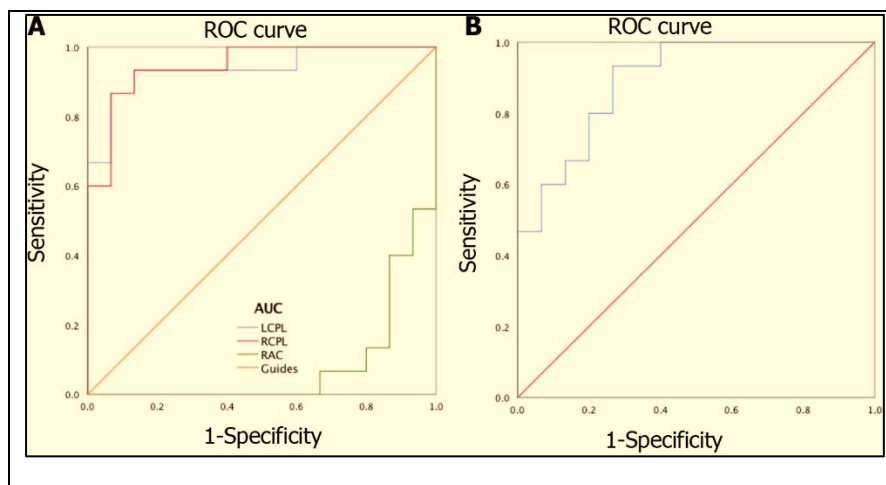


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Means of altered spontaneous brain activity between the diabetic retinopathy group and healthy controls.



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Receiver operating characteristic curve analysis of the mean amplitude of low-frequency fluctuation values for altered brain regions.

The best corrected visual acuity values of the DR group's eyes and the signal values of the bilateral calcarine were shown to have a positive association ( $r = 0.938$ ,  $P = 0.001$ ) in this study. It's possible that the patients' worse visual processing is reflected in the lower signal values of the bilateral calcarine fissures.<sup>2</sup> The cerebellum function is often thought to entail physical balance and motor coordination. According to Ferrari C et al<sup>3</sup>, we now have a better understanding of the unique effect of the cerebellum, especially its posterior lobe, on emotional processing, thanks to the development and deployment of neuroimaging technology in recent years. The ALFF values of the left and right posterior cerebellar lobes increased in this study. While we cannot verify that DR patients suffer from anxiety, we can speculate that anxiety may be present in DR patients who have visual or cognitive problems.

This research found that DR patients have certain aberrant spontaneous brain activity. The findings from these novel techniques could help to explain the neural mechanisms driving DR patients' clinical symptoms and lead to more accurate clinical diagnoses.

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