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ORIGINAL RESEARCH

Migraine Duration as a Potential Amplifier of Obesity

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Purpose: Migraine is a complex neurovascular disorder with obesity as a notable risk factor. This study aimed to investigate an under-researched area of the association between migraine duration and body composition.

Patients and Methods: Patients with migraine from a neurology outpatient department were enrolled and were categorized into four groups based on illness duration: 1 year, 1–5 years, 5–10 years, and >10 years. Patient demographics, blood biochemistry, and body composition data were collected and analyzed statistically.

Results: Patients with migraine were predominantly female, with lower education levels, significant work stress, poor sleep, and limited exercise. Longer migraine duration corresponded to increased obesity metrics. Notably, those patients with under 1 year of illness showed elevated blood lipid and liver function levels, whereas those with >10 years showed increased weight, waist circumference, body mass index, and fat content, despite higher physical activity. Significant positive correlation between obesity metrics and migraine duration was seen in patients who had migraine for >1 year.

Conclusion: Our findings indicate that protracted episodes of migraine could amplify obesity tendencies, underscoring the imperative of weight regulation in migraine intervention to diminish ensuing adiposity-associated hazards.

Keywords: migraine, illness duration, obesity, body composition

Introduction

Migraine is a globally prevalent chronic disease marked by intense pulsating headaches and symptoms such as nausea and photophobia.[1,2] Studies from China indicate its predominance in middle-aged urban women aged >30 years.[3,4] Lower socioeconomic status and limited education increase adverse outcomes, possibly due to insufficient awareness, medical access barriers, and treatment noncompliance.[5,6] Over-reliance on readily available over-The-counter analgesics can exacerbate symptoms, potentially transitioning episodic migraines to chronic forms.[7] Frequent analgesic use might deter patients from seeking formal medical advice. Moreover, the extended consequences of migraine, including anxiety, depression, and diminished activity, can affect the overall well-being of patients.

Obesity increases the risk of migraine. Individuals with a body mass index (BMI) ≥30 kg/m^2 show a markedly higher migraine prevalence than those with normal weight, and obese individuals are twice at risk than of their normal-weight counterparts [odds ratio (OR) 2.10 (1.39–3.12)].[8] This could be due to chronic inflammation and endocrine dysfunction observed in obese individuals.[9] Obese women had elevated levels of the pain-transmitting protein, calcitonin gene-related peptide (CGRP), compared with those having normal weight.[10] Rats with obesity and high CGRP levels also demonstrated more frequent events of cortical spreading depression (CSD), a slow neural and glial wave in the brain linked to ion imbalances.[11] Thus, the influence of obesity on migraine may arise from modulation of mechanisms, including endocrine pathways. However, CGRP is not considered as the gold standard for diagnosing migraines.

Body composition offers a more precise measure of obesity than body weight alone. Although BMI measures weight relative to height, the actual fat and muscle distribution is overlooked. With progressing of age, body fat percentage and

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muscle mass can shift without change in weight, leading to varied degrees of obesity for individuals with identical BMIs. Body composition analysis visually presents muscle, fat, water, and mineral proportions, indicating overall health. Major parameters, such as body fat percentage, visceral fat area, and waist-to-hip ratio, can precisely determine fat distribution and obesity assessment.[12] Techniques such as bioelectrical impedance analysis (BIA), dual-energy X-ray absorptiometry, and magnetic resonance imaging can measure body composition. Of these, BIA is highlighted for its simplicity, cost-effectiveness, and absence of radiation exposure.

Although obesity can elevate migraine risk, the influence of migraine duration on obesity levels or body composition variations among patients with different illness durations has not been elucidated yet. This study used the BIA technique to evaluate body composition, capturing metrics, such as BMI, waist circumference, fat-free mass (FFM), fat, protein, and minerals. This study aimed to discern lifestyle and body composition differences in patients with migraine based on their illness duration and to measure the effect of this duration on their degree of obesity.

Materials and Methods

Participants

The study complies with the Declaration of Helsinki, having been approved by the Independent Ethics Committee of the Second Affiliated Hospital of Fujian Medical University (IRB No. 2022–117) and involved the recruitment of adult migraine patients from the neurology outpatient department. Data collection encompassed sociodemographic details, exposure history, medical records, blood biochemistry, and body composition. Migraine-type evaluations were also conducted. They were categorized based on illness duration into four groups: Group 1 (G1, under 1 year), Group 2 (G2, 1 to 5 years), Group 3 (G3, 5 to 10 years), and Group 4 (G4, over 10 years). Exclusions were made for individuals under 18, those with physical conditions like diabetes or cardiovascular diseases, those pregnant or lactating, and those with mental disorders.

Medical history data provided insights into the demographic characteristics of participants, such as age, educational duration, and marital status. Details on exposure history, including occupational exposures and tobacco and alcohol consumption, and triggers like specific preceding events were also collected.

Migraine Diagnosis

Migraine types were determined by specialists, adhering to the International Classification of Headache Disorders, 3rd edition guidelines. Diagnosis relied on current medical history. During subsequent outpatient visits, ambiguous cases were advised to maintain a headache diary for a clearer diagnosis. This study included only primary migraine patients with or without aura and secondary migraine cases arising from substance or medication withdrawal.[2]

Blood Biochemistry Analysis

Participants provided a 2 mL venous blood sample, collected using standard procedures. The biochemical assessment was conducted using the Mindray BS-280 Fully Automated Chemical Analyzer (NMT, Shenzhen, China), which analyzed various parameters.

Body Composition Measurement

The body composition data were obtained and assessed by multifrequency tetrapolar Inbody S10 equipment (Biospace Co, Ltd., Seoul, Korea), the procedures were conducted in our prior research.[13] Pre-measurement protocols required fasting, bladder and bowel emptying, removal of metal jewelry, and lightweight clothing. Measurements were taken in seated or supine positions, ensuring proper contact with device electrodes. Evaluated indicators encompassed body weight, waist circumference, total body water (TBW), intracellular water (ICW), extracellular water (ECW), ECW/TBW ratio, body mass index (BMI), body fat mass (BFM), percent body fat (PBF), visceral fat area (VFA), fat mass (FFM), protein, skeletal muscle mass (SMM), lean balance, minerals, and phase angle (PhA).

Statistical Analysis

Statistical analysis was performed using SPSS 26.0 software. The normality of the data was assessed using the Kolmogorov–Smirnov test, while the homogeneity of variances was assessed using the Levene test. Normally distributed continuous data was described using mean ± standard deviation (X ± SD). The independent two-sample *t*-test was used to compare means between two groups (assuming homogeneity of variances), to determine if there were statistically significant differences in the measured variables between the groups. For non-normally distributed continuous data, variables were transformed to achieve normality or described using the median and interquartile range (P50, P75-P25). The Mann–Whitney *U*-test was used for comparison. Count data was expressed as percentages (%), and the chi-square test was used for comparisons. The relationship between disease duration and body composition was analyzed using Spearman's rank correlation. A p-value of < 0.05 was considered statistically significant.

Results

Characteristics of Patients

In this study, the final participants, were 10 men and 79 women, with an average age of 42.2±10.9 years. The participants were divided into four groups: G1 (15 participants), G2 (27 participants), G3 (19 participants), and G4 (28 participants). There were more female participants, aged between 34 and 51. No significant differences were found in age ($p = 0.155$) and height ($p = 0.595$) among the groups. Around 62.9% of the participants did not complete 9 years of compulsory education, and there were no significant differences in educational attainment among the groups ($p = 0.492$) (Table 1). The majority of patients (80.9%) reported engaging in light-intensity household chores as their

Table 1 Characteristics of the Participants

	Group 1 (n=15)	Group 2 (n=27)	Group 3 (n=19)	Group 4 (n=28)	χ^2	*p* value
Age(year)	44.2±10.2	38.4±9.9	41.0±10.1	44.7±11.5		0.155
Height(cm)	160.7±8.0	157.2±4.8	158.3±5.8	159.3±8.1		0.595
Gender					3.59	0.309
Female	13 (86.7%)	26 (96.3%)	15 (78.9%)	25 (92.9%)		
Male	2 (13.3%)	1 (3.7%)	4 (21.1%)	3 (7.1%)		
Educational duration					2.41	0.493
Less than 9 years	11 (73.3%)	14 (51.9%)	12 (63.2%)	19 (67.9%)		
More than 9 years	4 (26.7%)	13 (48.1%)	7 (36.8%)	9 (32.1%)		
Labor intensity					25.48	0.940
Mild	12 (80%)	23 (85.2%)	15 (78.9%)	22 (78.6%)		
Moderate	3 (20%)	3 (11.1%)	3 (15.8%)	6 (21.4%)		
Heavy	0 (0%)	1 (3.7%)	1 (5.3%)	0 (0%)		
Work stress					55.83	**<0.001**
None	12 (80.0%)	17 (63.0%)	8 (42.1%)	15 (53.6%)		
Mild	2 (13.3%)	5 (18.5%)	7 (36.8%)	6 (21.4%)		
Moderate	0 (0%)	1 (3.7%)	4 (21.1%)	7 (25%)		
Heavy	1 (6.7%)	4 (14.8%)	0	0		
Smoking history					2.67	0.445
Yes	0	0	1 (5.3%)	1 (3.6%)		
None	15 (100%)	27 (100%)	18 (94.7%)	27 (96.4%)		
Drinking history					2.67	0.445
Yes	1 (6.7%)	1 (3.7%)	1 (5.3%)	1 (3.6%)		
None	14 (93.3%)	26 (96.3%)	18 (94.7%)	27 (96.4%)		
Sleep quality					11.06	0.107
Satisfied	10 (66.7%)	10 (37.0%)	11 (57.9%)	10 (35.7%)		
Slight dissatisfaction	3 (20.0%)	13 (48.2%)	5 (26.3%)	7 (25.0%)		
Serious dissatisfaction	2 (13.3%)	4 (14.8%)	3 (15.8%)	11 (39.3%)		

(*Continued*)

Table 1 (Continued).

	Group 1 (n=15)	Group 2 (n=27)	Group 3 (n=19)	Group 4 (n=28)	χ^2	*p* value
Exercise intensity					25.48	**<0.001**
None	7 (46.7%)	21 (77.8%)	18 (94.7%)	13 (46.4%)		
Mild	8 (53.3%)	4 (14.8%)	0	11 (39.3%)		
Moderate	0	2 (7.4%)	1 (5.3%)	4 (14.3%)		
Heavy	0	0	0	0		
Weekly exercise frequency					23.52	**0.001**
0	8 (53.3%)	22 (81.5%)	18 (94.7%)	12 (42.9%)		
1–2	1 (6.7%)	2 (7.4%)	0 (0.0%)	8 (28.6%)		
3–5	6 (40.0%)	3 (11.1%)	1 (5.3%)	8 (28.6%)		

Notes: Group 1: Migraine patient for a period less than 1 year, Group 2: Migraine patient for period 1–5 years, Group 3: Migraine patient for period 5–10 years, Group 4: Migraine patient for period more than 10 years. Bolded values indicate that < 0.05 is considered to possess statistical significance.

primary occupation. Participants in G3 and G4 had a higher prevalence of individuals experiencing stress ($p < 0.001$), with 41.6% perceiving mild to severe work-related stress (Table 1). Most patients in all groups reported no work-related stress. However, some patients, especially who had been suffering from migraines for over five years, expressed in the questionnaire the pressure caused by chronic migraines leading to inadequate sleep and decreased work efficiency, which is also a contributing factor to the perception of work-related stress the subjects in this study, even when engaged in light labor.

Only 12.4% of the participants reported experiencing menstrual-related headaches, and there were no significant differences in the prevalence of menstrual-related headaches among the groups ($p = 0.187$). A small percentage of participants had a history of smoking (2.2%) and alcohol consumption (4.4%). More than half of the participants (53.9%) expressed dissatisfaction with their sleep quality, with the highest level observed in the G4 group, indicating the poorest sleep quality. However, there were no significant differences in sleep problems among the groups ($p = 0.107$). The majority of patients (66.3%) do not have a regular exercise habit, and those who engage in exercise mainly participate in light-intensity activities such as walking. G2 and G3 had the lowest levels of physical activity ($p < 0.001$) and exercise frequency ($p = 0.001$) (Table 1).

Blood Biochemistry

Table 2 shows significant differences in blood biochemistry results among the different groups. The following parameters exhibited significant differences: total protein ($p = 0.009$), alanine aminotransferase (ALT) ($p = 0.001$), aspartate aminotransferase (AST) ($p = 0.014$), AST/ALT ($p = 0.046$), alkaline phosphatase (ALP) ($p = 0.024$), γ-glutamyl transpeptidase (γ-GT) ($p < 0.001$), cholesterol ($p = 0.005$), low-density lipoprotein-cholesterol (LDL-c) ($p = 0.001$), apolipoprotein-B (APB) ($p = 0.007$), and APB: APA ($p = 0.04$).

G1 had the highest values in total protein, ALT, AST, γ-GT, cholesterol, LDL-c, and APB, which were significantly higher than those of the other three groups. However, no significant differences were observed among the other three groups. ALP levels were significantly higher in G1 compared to G2 ($p = 0.005$) and G3 ($p = 0.029$) but did not differ significantly from G4. The APB: APA ratio in G1 was higher than that of G3 ($p = 0.015$) and G4 ($p = 0.049$). The AST/ALT ratio in G1 was the lowest and significantly lower than G2 and G3 ($p = 0.015, 0.007$), but did not differ significantly from G4 (Table 2).

Body Composition

The results demonstrate significant differences in body weight ($p = 0.041$) and waist circumference ($p = 0.043$) among the groups. Both G1 and G4 had higher values compared to G2 and G3 in terms of weight and waist circumference. Specifically, G4 displayed the highest values for waist circumference ($p = 0.012$) and weight ($p = 0.006$) compared to G2 (Table 3, Figure 1). However, no significant differences were observed in other body composition indicators such as TBW, ICW, ECW, ECW/TBW, PBF, VFA, FFM, protein, SMM, mineral, and PhA (Table 3).

Table 2 Analysis of Blood Profiles Across Different Periods Cohort Migraine Patients

	Group 1	Group 2	Group 3	Group 4	*p* value	post hoc Test *p* value		
						G1 vs G2	G1 vs G3	G1 vs G4
Total protein (g/L)	77.14 ± 1.82	71.25 ± 3.39	71.60 ± 3.97	73.08 ± 2.53	**0.009**	**0.001**	**0.005**	**0.033**
Albumin (g/L)	48.06 ± 0.88	45.34 ± 2.47	46.53 ± 2.11	45.75 ± 2.34	0.125	NA	NA	NA
Globulin (g/L)	29.08 ± 1.72	25.91 ± 2.88	25.08 ± 3.82	27.33 ± 3.34	0.118	NA	NA	NA
Total bilirubin (μmol/L)	11.38 ± 6.47	9.60 ± 3.57	9.63 ± 2.60	8.91 ± 4.40	0.761	NA	NA	NA
Direct bilirubin (μmol/L)	4.30 ± 1.74	3.75 ± 1.05	4.13 ± 1.05	3.82 ± 1.71	0.816	NA	NA	NA
Indirect bilirubin (μmol/L)	7.08 ± 4.76	5.86 ± 2.61	5.50 ± 1.69	5.09 ± 2.74	0.660	NA	NA	NA
Alanine aminotransferase (U/L)	36.82 ± 28.57	13.01 ± 4.91	12.50 ± 4.84	15.85 ± 5.81	**0.001**	**<0.001**	**<0.001**	**0.002**
Aspartate aminotransferase (U/L)	29.06 ± 20.64	14.96 ± 4.20	15.43 ± 2.35	17.74 ± 4.79	**0.014**	**0.002**	**0.006**	**0.02**
AST/ALT	0.84 ± 0.25	1.23 ± 0.36	1.32 ± 0.28	1.16 ± 0.15	**0.046**	**0.015**	**0.007**	0.062
Alkaline phosphatase(U/L)	85.88 ± 26.03	58.68 ± 11.27	63.11 ± 16.12	72.83 ± 22.75	**0.024**	**0.005**	**0.029**	0.199
γ-GT (U/L)	53.86 ± 27.17	17.23 ± 8.71	18.90 ± 8.71	20.61 ± 11.17	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Cholesterol (mmol/L)	5.77 ± 1.04	4.71 ± 0.65	4.30 ± 0.60	4.55 ± 0.57	**0.005**	**0.005**	**0.001**	**0.004**
Triglyceride (mmol/L)	1.65 ± 1.39	1.50 ± 0.88	0.95 ± 0.28	1.79 ± 1.64	0.458	NA	NA	NA
HDL-c (mmol/L)	1.45 ± 0.43	1.31 ± 0.27	1.48 ± 0.30	1.35 ± 0.41	0.646	NA	NA	NA
LDL-c (mmol/L)	3.83 ± 0.81	3.02 ± 0.59	2.58 ± 0.50	2.59 ± 0.19	**0.001**	**0.007**	**<0.001**	**<0.001**
Apolipoprotein-A (g/L)	1.51 ± 0.23	1.37 ± 0.14	1.50 ± 0.24	1.43 ± 0.22	0.323	NA	NA	NA
Apolipoprotein-B (g/L)	1.19 ± 0.24	0.97 ± 0.19	0.82 ± 0.17	0.84 ± 0.17	**0.007**	**0.03**	**0.002**	**0.003**
APB: APA	0.80 ± 0.19	0.72 ± 0.17	0.56 ± 0.14	0.61 ± 0.19	**0.040**	0.348	**0.015**	**0.049**
Blood urea nitrogen (mmol/L)	5.44 ± 2.34	4.27 ± 1.1	4.04 ± 0.67	5.05 ± 1.03	0.132	NA	NA	NA
Creatinine (μmol/L)	60.66 ± 7.91	59.13 ± 10.4	56.8 ± 9.96	67.26 ± 8.25	0.161	NA	NA	NA
Uric acid (μmol/L)	333.20 ± 76.81	328.56 ± 81.24	320.75 ± 51.34	349.88 ± 73.95	0.874	NA	NA	NA
Glucose (mmol/L)	5.73 ± 1.37	5.27 ± 0.58	5.27 ± 0.66	5.60 ± 0.52	0.505	NA	NA	NA
Lactate dehydrogenase (U/L)	174.64 ± 19.13	153.98 ± 35.23	155.99 ± 38.17	137.04 ± 17.00	0.228	NA	NA	NA
Creatine kinase (U/L)	81.78 ± 28.71	73.03 ± 37.41	79.61 ± 39.50	82.45 ± 49.27	0.938	NA	NA	NA
Creatine kinase MB (U/L)	11.62 ± 2.95	12.48 ± 4.09	11.56 ± 2.98	11.63 ± 3.27	0.908	NA	NA	NA
Potassium (mmol/L)	4.19 ± 0.51	4.05 ± 0.42	4.25 ± 0.28	4.15 ± 0.27	0.665	NA	NA	NA
Sodium (mmol/L)	140.36 ± 1.40	139.74 ± 1.62	139.3 ± 1.48	140.21 ± 1.27	0.538	NA	NA	NA
Calcium (mmol/L)	2.41 ± 0.08	2.32 ± 0.09	2.28 ± 0.09	2.31 ± 0.07	0.065	NA	NA	NA
Phosphorus (mmol/L)	1.03 ± 0.16	1.10 ± 0.13	1.09 ± 0.07	1.13 ± 0.16	0.616	NA	NA	NA
Magnesium (mmol/L)	0.93 ± 0.06	0.87 ± 0.05	0.88 ± 0.06	0.92 ± 0.05	0.052	NA	NA	NA

Notes: Group 1: Migraine patient for a period less than 1 year, Group 2: Migraine patient for period 1–5 years, Group 3: Migraine patient for period 5–10 years, Group 4: Migraine patient for period more than 10 years. A/G: albumin/globulin; AST/ALT: aspartate aminotransferase/alanine aminotransferase; γ-GT: γ-glutamyl transpeptidase; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; APB: APA: apolipoprotein-B: apolipoprotein-A; BUN/CREA: blood urea nitrogen/ creatinine. Bolded values indicate that < 0.05 is considered to possess statistical significance.

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Table 3 Analysis of Body Composition Across Different Periods Cohort Migraine Patients

	Group 1 (n=15)	Group 2 (n=27)	Group 3 (n=19)	Group 4 (n=28)	*p* value	post hoc Test *p* value		
						G1 vs G4	G2 vs G4	G3 vs G4
Weight(kg)	64.47 ± 16.83	56.67 ± 11.27	58.87 ± 6.58	64.80±10.68	**0.041**	0.93	**0.012**	0.094
Waist Cir. (cm)	83.11 ± 8.03	79.35 ± 10.51	81.88 ± 7.43	86.66 ± 9.56	**0.043**	0.237	**0.005**	0.093
ICW (kg)	21.14 ± 6.38	18.29 ± 2.69	19.00 ± 2.66	20.05 ± 3.74	0.118	NA	NA	NA
ECW (kg)	12.65 ± 3.66	11.12 ± 1.53	11.38 ± 1.52	12.09 ± 1.95	0.123	NA	NA	NA
TBW (kg)	33.79 ± 10.03	29.41 ± 4.20	30.38 ± 4.16	32.14 ± 5.68	0.119	NA	NA	NA
ECW/TBW	0.37 ± 0.005	0.38 ± 0.006	0.38 ± 0.007	0.38 ± 0.007	0.184	NA	NA	NA
Protein	9.17 ± 2.77	7.90 ± 1.16	8.21 ± 1.160	8.66 ± 1.62	0.112	NA	NA	NA
Mineral (kg)	3.13 ± 1.67	2.70 ± 0.34	2.74 ± 0.32	2.95 ± 0.52	0.112	NA	NA	NA
FAT (kg)	18.40 ± 5.95	16.66 ± 7.11	17.53 ± 574	21.04 ± 8.04	0.134	NA	NA	NA
SLM (kg)	43.47 ± 12.94	37.79 ± 5.43	39.09 ± 5.39	41.33 ± 7.40	0.118	NA	NA	NA
FFM (kg)	46.07 ± 13.96	40.02 ± 5.68	41.34 ± 5.60	43.76 ± 7.81	0.117	NA	NA	NA
TBW/FFM	73.40 ± 0.29	73.48 ± 0.25	73.49 ± 0.31	73.46 ± 0.20	0.733	NA	NA	NA
SMM (kg)	25.58 ± 8.32	21.86 ± 3.50	22.78 ± 3.47	24.16 ± 4.88	0.118	NA	NA	NA
PBF (%)	28.56 ± 7.14	28.40 ± 7.28	29.49 ± 8.31	31.90 ± 8.70	0.386	NA	NA	NA
BMI (kg/m^2)	24.70 ± 4.05	22.86 ± 4.51	23.77 ± 3.42	25.57 ± 4.15	0.111	NA	NA	NA
AC (cm)	30.91 ± 2.93	29.11 ± 4.29	30.05 ± 2.98	31.56 ± 3.22	0.079	NA	NA	NA
AMC (cm)	26.75 ± 2.39	25.15 ± 3.42	25.91 ± 2.48	26.86 ± 2.29	0.112	NA	NA	NA
VFA (cm^2)	77.25 ± 31.28	73.07 ± 38.96	78.34 ± 34.97	97.28 ± 46.32	0.135	NA	NA	NA
SMM/VFA	0.40 ± 0.26	0.38 ± 0.20	0.62 ± 1.28	0.33 ± 0.24	0.472	NA	NA	NA
BMR (kcal)	1365.40 ± 301.57	1234.35 ± 122.53	1263.06 ± 121.04	1315.41 ± 168.73	0.116	NA	NA	NA
SMI (%)	7.21 ± 1.33	6.51 ± 1.03	6.76 ± 0.98	6.97 ± 0.84	0.167	NA	NA	NA
Phase Angle	6.25 ± 0.63	5.77 ± 0.81	6.04 ± 0.78	5.93 ± 0.76	0.261	NA	NA	NA

Notes: Group 1: Migraine patient for a period less than 1 year, Group 2: Migraine patient for period 1–5 years, Group 3: Migraine patient for period 5–10 years, and Group 4: Migraine patient for period more than 10 years. Bolded values indicate that < 0.05 is considered to possess statistical significance.
Abbreviations: ICW, intracellular water; ECW, extracellular water; TBW, total body water; SLM, soft lean mass; FFM, fat-free mass; SMM, skeletal muscle mass; PBF, percent body fat; BMI, body mass index; AC, arm circumference; AMC, arm muscle circumference; VFA, visceral fat area; BMR, basal metabolic rate; SMI, skeletal muscle mass index.

Figure 2 shows an increasing trend in body weight, waist circumference, fat, and BMI among the three groups, except for Group 1. Group 4 has significantly higher body weight ($p = 0.012$), waist circumference ($p = 0.005$), fat ($p = 0.025$), and BMI ($p = 0.019$) compared to Group 2. Figure 3 shows the correlations between weight, waist circumference, BMI, and fat of migraine patients for more than 1 year. The other three groups showed significant differences in weight ($r = 0.509$, $p < 0.0001$), waist circumference ($r = 0.479$, $p < 0.0001$), BMI ($r = 0.467$, $p < 0.0001$), and fat ($r = 0.366$, $p = 0.0017$), indicating a gradual

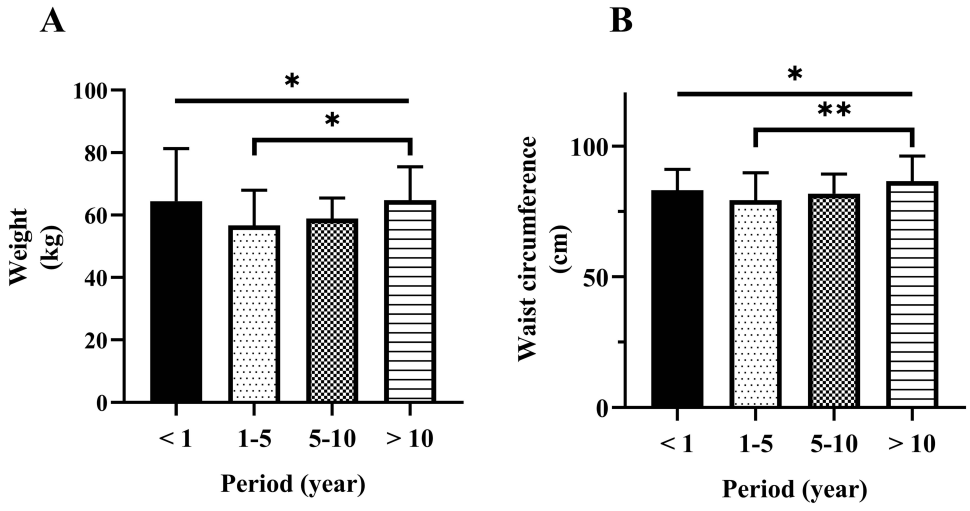

Figure 1 Body weight (**A**) and waist circumference (**B**) of cohort migraine patients. *p <0.05, **p <0.01.

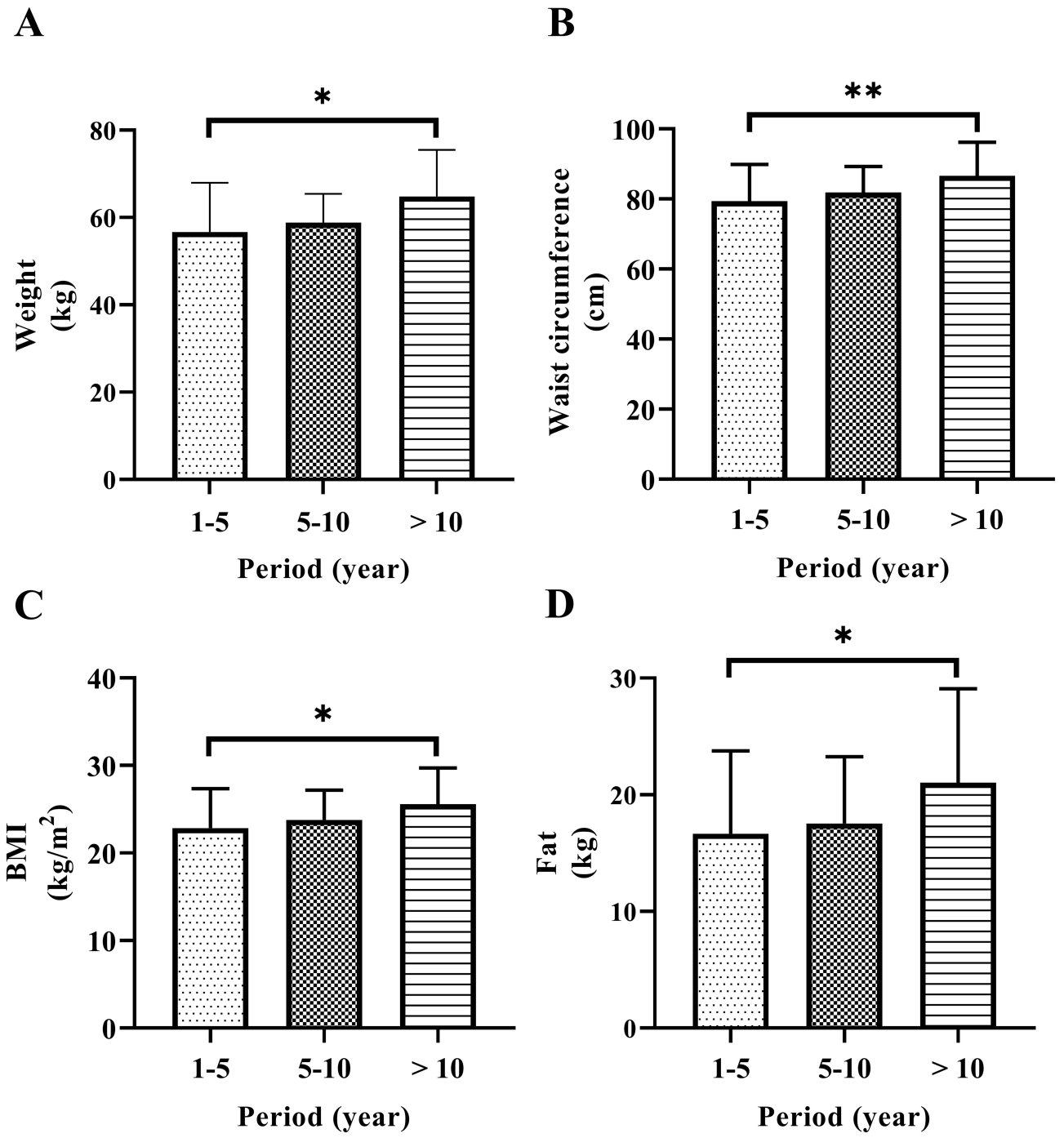

Figure 2 Body weight (**A**), waist circumference (**B**), body mass index (BMI) (**C**), and fat (**D**) of cohort migraine patients. *p<0.05, **p<0.01.

increasing trend. Furthermore, a positive correlation was observed between the increase in these indicators and the duration of the disease in these three groups. Considering the potential impact of work-related stress and exercise on body weight, comparable data were grouped and contrasted based on similar levels of work-related stress and exercise habits. Similar results were observed in the subgroup with no work-related stress and no exercise habits, as in the ungrouped data.

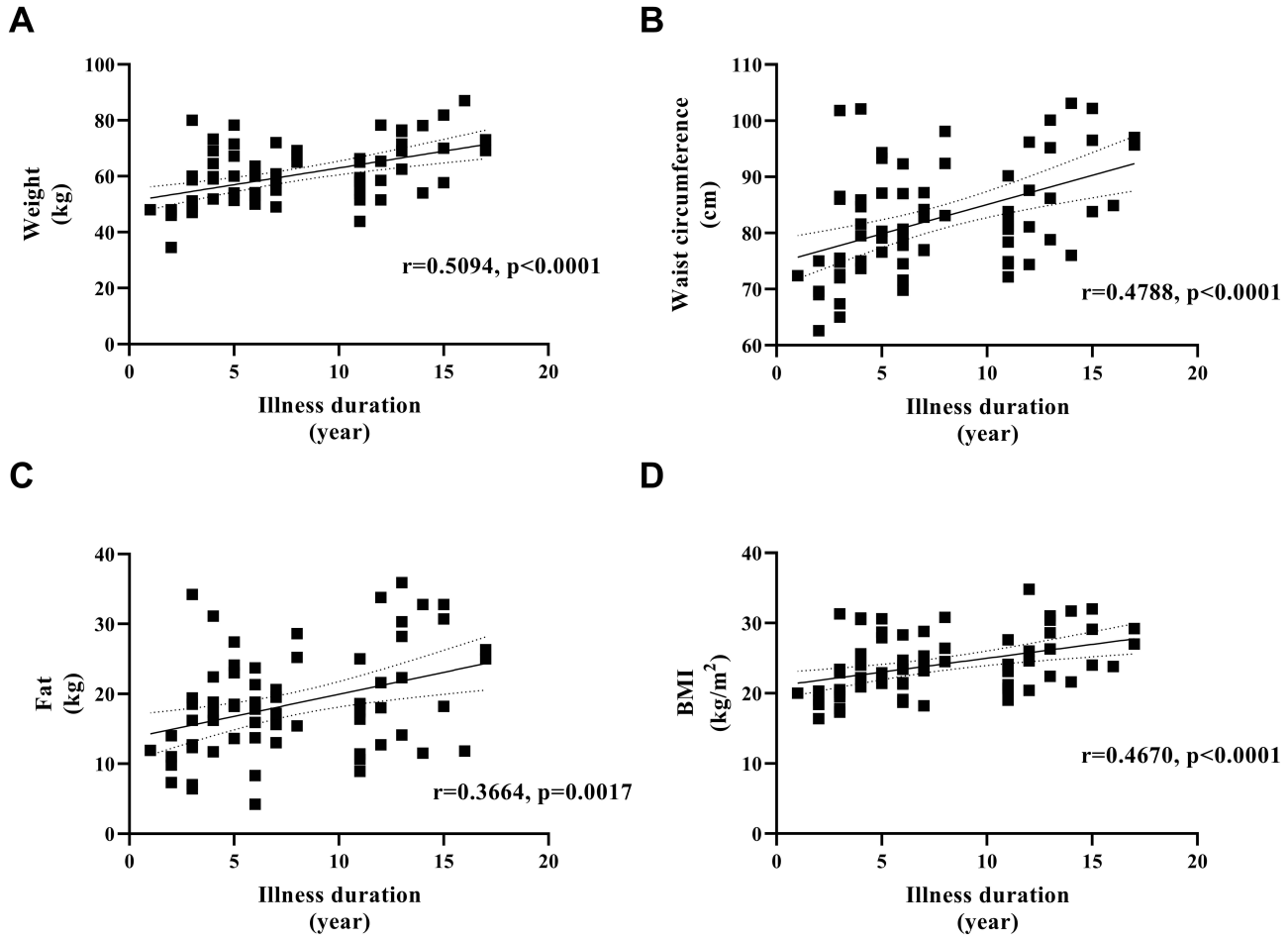

Figure 3 The correlation between the duration of illness and weight (**A**), waist circumference (**B**), fat (**C**), body mass index (BMI) (**D**) of migraine patients for a period of more than 1 year.

Discussion

Present study mainly identified patients seeking outpatient care for migraines, predominantly middle-aged women, with approximately 50% being overweight or obese, with education levels up to elementary or junior high school, and mostly homemaker individuals. Life stress, sleep disturbances, and a sedentary lifestyle were commonly reported by the patients. Notably, a significant increase in weight, waist circumference, BMI, and body fat correlated with disease duration, even after adjusting for height and age.

This study primarily included female participants aged 34–51 years, consistent with a previous study.[3] The increased occurrence of migraines in women has been linked to ovarian sex hormone secretion, leading to a heightened migraine frequency in women of childbearing age compared with men. Conversely, the migraine rates of postmenopausal and prepubescent women were similar to men.[14] Lower estrogen levels reduce migraine symptoms, possibly due to the effect of sex hormones on cerebral circulation, reducing vascular tone and increasing cerebral blood volume.[15] Women experience longer migraines durations and more frequent recurrences,[16] along with extended periods of activity limitation due to migraines compared with men, leading to greater prevalence of headache-related disability among women.[17,18]

Our findings revealed that chronic migraine adversely affects sleep quality. Sleep disturbances, including trouble initiating sleep and premature awakenings were reported by majority of patients, resulting in overall dissatisfaction in sleep quality. Notably, those with migraine durations >10 years experienced poor sleep quality, underscoring the negative impact of long-term headaches on sleep. Lack of sleep triggers migraine by disrupting biological rhythms, hormonal balance, and increasing inflammatory factors.[19] Additionally, poor sleep quality in patients with migraine is frequently

linked with adverse emotional states, such as anxiety and depression.[19] Migraine attacks prolong sleep onset and shorten sleep duration, which reduces sleep quality and exacerbates anxiety and depression, that can cause migraines, complicate treatment, and lead to relapses.[20] Sleep deprivation and anxiety are also recognized risk factors for obesity.[21] Although neither is a major cause of migraines, it can further exacerbate the frequency and severity of migraine headaches.[22]

A few patients in this study reported work-related stress. Different results have been observed in previous studies of psychosocial factors and body weight in the workplace, but a slight correlation was found in men with long working hours.[23] The patients in this study did not report long working hours, and thus work-related stress was not a cause of obesity in migraine patients.

Notably, the study population exhibited a lack of exercise, primarily due to migraine-related discomfort deterring physical activity, resulting in inadequate exercise and aggravated obesity. Exercise plays a crucial role in migraine treatment and prevention. Individuals lacking physical activity are at a higher risk of migraines, whereas regular exercise diminishes migraine risk and occurrence frequency.[24] Interestingly, it was found that patients with >10 years of illness demonstrated a significantly increased exercise intensity and frequency, indicating that prolonged headache experience might increase disease awareness and motivate beneficial physical engagement.

Currently, most migraine medications, such as sodium valproate and flunarizine, except for topiramate, are associated with weight gain. The participants in our study often resorted to irregular migraine treatments, especially using over-The-counter pain relievers, such as aspirin, ibuprofen, and acetaminophen, during headaches. Notably, these medications did not significantly affect body weight. However, our findings revealed that approximately 50% of patients had a BMI ≥24, classifying them as overweight or obese, which is consistent with existing research indicating a correlation between increased body weight and a higher migraine risk.[8] Significant differences were seen in the weight and waist circumference among patients with migraine and varying illness durations. Specifically, weight, waist circumference, BMI, and body fat percentage showed positive correlations with illness duration among those with migraine >1 year. International population surveys validate that obesity can increase the risk of chronic migraines[25–27] or intensify headache frequency and severity,[28] possibly due to obesity-related chronic inflammation and metabolic dysregulation.[29] Chronic inflammation in obesity might affect the trigeminal nerve and meninges.[30] Obese rats exhibited heightened CGRP release from the trigeminal nerve under harmful stimuli, reducing the headache threshold.[31] The trigeminal nerve is central to pain perception in the anterior two-thirds of the head and plays a crucial role during headache.[32] Concurrently, CSD between the meninges and cortex is a key mechanism in migraine with aura, and it can also be affected by inflammation.[33] Inflammation-induced alterations in K^+ channels may also explain the increased CSD production in obese rats.[34] Furthermore, the unhealthy lifestyles of obese patients, such as a high-fat diet, sedentary habits, and irregular sleep, combined with cumulative daily stress from work and social pressures, have been linked to migraine onset and progression. These daily stressors can also worsen symptoms and influence migraine frequency and severity via neural regulation, inflammatory responses, and blood rheology.[35]

Although our study did not show significant differences in the inflammatory markers in the patient's blood tests, a previous study has confirmed a close association between migraines and inflammation. The pathophysiology of migraines involves proinflammatory cytokines, including interleukin-6 (IL-6), interleukin-1β (IL-1β), and tumor necrosis factor-α (TNF-α). These markers undergo changes at serum levels of patients with migraine,[36] with alterations in TNF-α levels observed in the serum and/or urine samples of some patients with migraine during and between attacks.[36,37] However, these data are controversial. Furthermore, migraines were speculated to be the result of neurogenic inflammation.[36] Dural neurogenic inflammation is considered a driving factor for migraine attacks. Studies reveal that neurogenic inflammation contributes to increased blood–brain barrier permeability, leukocyte infiltration, glial cell activation, and inflammatory cytokines secretion.[36] On the other hand, increased adipose tissue mass and adipocyte hypertrophy are closely associated with the secretion of inflammatory mediators, such as cytokines, chemokines, and acute-phase proteins.[38] The plasma levels of TNF-α, IL-6, and C-reactive protein (CRP) are elevated in overweight individuals.[39] Therefore, in migraine patients with an inflammation history, increased inflammatory cytokine levels may be a contributing factor to their obesity, whereas the exacerbation of inflammatory conditions may also be related to more frequent and severe migraine attacks, eventually transitioning to chronic migraines.[40]

The patients enrolled in this study were not diagnosed with any metabolic disorders, such as insulin resistance. However, the presence of abnormal biochemical markers indicated underlying metabolic disturbances. In the subgroup experiencing migraines <1 year, blood biochemical tests revealed lipid-associated markers including elevated levels of cholesterol, LDL-C, APB, and the APB:APA ratio. Notably, LDL-C showed a positive correlation with body adiposity index, indicating its association with obesity.[41] The surge in cholesterol and APB indicates compromised adipocyte functionality and enlargement, implying severe obesity and disrupted lipid metabolism in this particular group.[42] Additionally, liver function markers including ALT, AST, γ-GT, and alkaline phosphatase, were significantly elevated. Moreover, elevated alanine aminotransferase and aspartate aminotransferase levels indicated liver cell damage and cholestasis-related injury.[43] These outcomes indicated that the subgroup with migraine <1 year showed more pronounced liver damage than the other groups, further underlining severe obesity and metabolic disturbances. The common characteristics of G1 were higher age, weight, BMI, and waist circumference, indicating severe obesity in G1. This explains the higher values in their biochemical test results, which indicated the presence of obesity before headache onset, potentially influencing migraine severity and occurrence.[28,44]

Notably, the severity of obesity and duration of illness showed a clear positive correlation after removing G1. The degree of obesity in the G1 group was comparable to that of the G4 group, and no significant age difference was observed between the two groups, with the age distribution relatively close to that of the other groups. Although female aging coupled with reduced menstruation and decreased hormone levels may lead to weight gain and increased body fat, age was not an influential factor for obesity in migraine patients in this study.[45] This result may be related to the severity of the headache at the time the patient seeks medical attention. Blood test results indicated that patients with migraine <1 year may have been obese and had more severe headaches before their migraine attacks. In contrast, patients with a longer duration of illness did not seek medical attention in a timely manner because their previous migraine symptoms were mild and did not significantly affect their work and daily life, and sought medical help only after their symptoms worsened, thus prolonged migraines led to the development of obesity in the patients.

The shared mechanism underlying migraine and obesity may involve interactions at the central and peripheral levels. The hypothalamus, which stimulates and inhibits feeding, also regulates gastrointestinal function. Hypothalamic-related symptoms, such as food cravings, emotional disturbances, and sleep issues are often experienced by patients with migraine.[46] Imaging studies have shown hypothalamic activation during migraine attacks may contribute to hyperphagia and subsequent weight gain.[47] Additionally, the hypothalamic release of feeding-related peptides and proteins, including serotonin, orexin, and leptin, play role in migraine pathophysiology, potentially increasing the migraines incidences in individuals with obesity.[48] Peripherally, the association between migraine and obesity is linked to the release of inflammatory factors from the adipose tissue in obesity cases.

This study has few limitations. First, the cross-sectional design hindered our ability to track body composition changes before and after illness onset. A longitudinal approach in future studies could provide more insight into the migraine–obesity connection. Second, the limited sample size raises concerns regarding potential bias in the results, indicating the requirement for larger-scale research with more participants to support the validity of the study. The gender ratio and age range of the participants in this study were similar to those in previous relevant surveys, indicating generalizability to the migraine population. However, the cases were limited to the Quanzhou region, which may limit the generalizability to populations in other areas. Thus, more external data collection through multicenter research in the future could validate our study results. Our findings support clinical guidelines for migraine prevention, emphasizing behavioral interventions and reasonable medication use for preventing the progression from episodic to chronic migraines. Third, the lack of headache severity quantification in this study restricted our understanding of variations in disease severity across different groups. Future research should consider including headache severity, frequency, and duration for a more comprehensive evaluation of patients with migraine.

Conclusion

Present study identified that the key characteristics in patients with migraine were female sex, lower education, high work stress, poor sleep, and little exercise. A clear correlation was seen between migraine duration of >1 year and increased

body metrics, such as weight and BMI. Shorter migraine history was linked to altered lipid and liver function, indicating the potential role of obesity in the worsening of migraine severity, indicating a possible selection bias because less obese individuals may seek less medical care. Despite existing research, the precise relationship between chronic migraine and obesity requires further high-quality, prospective studies for a clearer understanding and improved patient care.

Data Sharing Statement

The data used to support the findings of this study have been included in this article.

Ethics Approval and Consent to Participate

This study was performed in according with the Declaration of Helsinki and was approved by the Research Ethics Committee of the Second Affiliated Hospital of Fujian Medical University (IRB No. 2022-117). Participants provided written informed consent before initiating the study.

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Disclosure

The authors report no conflicts of interest in this work.

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