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The obesity paradox in primary Sjögren's disease: immunometabolic associations of chemerin, platelet count, and statin use

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Introduction: Sjögren's disease is characterized by autoimmune destruction of exocrine glands. Obesity generally worsens the course of many diseases; however, earlier observations in our cohort suggested a paradoxically lower disease activity (ESSDAI) in overweight/obese patients. This cross-sectional study aimed to investigate potential mechanisms underlying these findings.

Methods: Chemerin and oxidized low-density lipoprotein (oxLDL) levels were measured in a subset of regularly followed patients (n=75). Patients were stratified by body mass index (BMI): BMI <25 kg/m² ("non-obese", n=27) and BMI ≥25 kg/m² ("overweight/obese", n=48). Demographic, laboratory, and immunological parameters, disease activity (ESSDAI), extraglandular manifestations, and treatments were compared using biostatistical analyses.

Results: Chemerin and oxLDL levels did not differ significantly between groups. ESSDAI was significantly lower in overweight/obese patients (5.04 vs. 2.76; p=0.04), while complement c3 levels were higher (1.20 vs. 1.46 g/L; p<0.001). Across all patients, chemerin positively correlated with BMI, age at diagnosis, c3, c4, CRP, platelet count, and leukocyte count. Hemoglobin and hematocrit were higher in overweight/obese patients, whereas neutrophil ratio was lower and lymphocyte ratio slightly higher. Statin therapy was also more frequent in the overweight/obese group (p=0.04). In this group, BMI and platelet count independently predicted chemerin levels, while platelet count predicted chemerin in normal-weight patients.

Conclusion: Despite its positive correlation with BMI, chemerin levels were not significantly higher in overweight/obese patients, suggesting relatively lower levels. This may partly explain their more favorable immunological profile. Increased statin use may also contribute through anti-inflammatory effects.

KEYWORDS

adipokine, chemerin, obesity, oxLDL, Sjögren's disease, statin

1 Introduction

Sjögren's disease is characterized by the autoimmune-mediated destruction of ductal epithelial cells, which leads to various symptoms. Most of them are related to the dysfunction of exocrine glands, such as xerostomia, xerophthalmia, pancreas dysfunction, skin dryness, vaginitis sicca, etc. Besides, it can also cause numerous extraglandular manifestations, for instance, non-erosive polyarthritis, central and peripheral nervous system manifestations, interstitial lung disease, muscular involvement, nephropathy, vasculitis, and different types of autoimmune cytopenia among others (1–3). It is also important to mention accelerated atherosclerosis, which is proved to be a serious complication in autoimmune diseases, researched mainly in systemic lupus erythematosus and rheumatoid arthritis, but it is present in Sjögren's disease as well, further aggravating its cardiovascular risk (4–7).

Obesity is known to influence a wide range of diseases and is a basic feature of the assessment of risk factors (8, 9), exceeding even tobacco use at this point (10). In our prior paper, we observed that Sjögren's patients with a normal body weight have higher disease activity compared to obese ones (11). Subsequently, extensive literature research was conducted to unravel the potential causes behind these findings. Three key contributing factors can be assumed. First of all, the obesity paradox is a well-studied phenomenon, which states that metabolically healthy obese individuals have better survival rates in numerous diseases than patients with a normal weight who otherwise live an unhealthy lifestyle (12–14). Secondly, the effect of statin therapy must be mentioned, although in this paper we are not focusing on that, since it was revised in our previous study. The majority of our overweight/obese patients were undergoing contemporary statin treatment, while such medication was used by only a small percentage of the non-obese group. Statins are well recognized for their pleiotropic anti-inflammatory effect, which may ameliorate the clinical course of Sjögren's disease. By suppressing certain inflammatory pathways and inflammasome activation, they mitigate the risk of endothelial dysfunction (15–18). The effects of these drugs have been studied in autoimmune diseases with promising results, including rheumatoid arthritis, systemic lupus erythematosus, antiphospholipid syndrome and vasculitis (19–21). The third suspected cause behind our results is the role of certain adipokines which provided the idea for our current research.

Adipokines are secreted by the adipose tissue, which essentially acts like an endocrine organ, meaning that these molecules are biologically active and influence the operation of several organs. When a patient is severely obese, the endocrine function of the adipose tissue shifts to an adverse way secreting more pro-inflammatory adipokines compared to anti-inflammatory ones. This leads to the aggravation of local and systemic inflammation, which contributes to the progression of several diseases linked to obesity and also interferes with autoimmune mechanisms (22–25). Our study focused on chemerin and oxidized low-density lipoproteins (oxLDL).

Chemerin is an adipokine which serum levels correlate positively with body mass index (BMI). It plays an important role in inflammatory processes, and its receptors, including chemokine-like

receptor-1 (CMKLR1), G-protein coupled receptor-1 (GPR1) and C-C-motif chemokine like receptor (CCRL2), are expressed by adipocytes and inflammatory cells. Chemerin contributes to immune-cell recruitment and immune homeostasis, particularly through its effects on innate immune cells such as dendritic cells and macrophages. It has also been implicated in atherogenesis and metabolic regulation, including glucose metabolism, insulin sensitivity, adipogenesis, and angiogenesis (26–29). More broadly, emerging evidence suggests that obesity-associated inflammation involves complex communication between metabolic and immune organs rather than adipose tissue acting in isolation. The liver-spleen axis has recently been described as an important immunometabolic pathway, in which splenic immune-cell activation and monocyte trafficking through the portal circulation can influence hepatic inflammation and fibrogenesis, while hepatic signals can reciprocally modulate systemic and splenic immune activity (30). This concept further supports the potential relevance of adipokines and other circulating inflammatory mediators in systemic immune-metabolic regulation. In the present study, we therefore focused on chemerin and oxidized low-density lipoproteins (oxLDL).

Oxidized low density lipoproteins are known to modulate inflammatory pathways in several ways, contributing to atherogenesis, influencing the operation of macrophages, plaque formation and plaque instability as well. They also have antigenic potential, through pattern recognition receptors (PRRs), they can secrete cytokines and can bind to specific antibodies forming immune complexes activating inflammatory cells. Therefore, the role of oxLDL is mainly considered disadvantageous, however, recent studies suggest that it may serve as a potential therapeutic target for the prevention of thromboembolism, although more research is needed in that area (31–35).

In this present study, we aimed to further investigate the etiology of lower disease activity of overweight/obese patients. Therefore, we researched whether obesity-associated immune-metabolic factors explain this phenomenon and explored immune-metabolic heterogeneity in Sjögren's disease.

2 Materials and methods

2.1 Patient enrolment

Out of our regularly followed patients, chemerin and oxLDL levels were assessed in a subset of 75 people. All patients gave informed consent to participate. Patients were stratified into two groups based on body mass index (BMI): those with a BMI < 25 kg/m² were classified as 'non-obese' (n=27), while those with a BMI ≥ 25 kg/m² were categorized as 'overweight/obese' (n=48). In the non-obese group, the median age was 61, while in the overweight/obese group it was 60. All the patients were women. Demographic parameters (gender, age at diagnosis of Sjögren's disease), complete blood count, kidney and liver function tests, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), triglyceride, cholesterol levels, immunological parameters (anti-SS-A, anti-SS-B, complement

levels), EULAR Sjögren's syndrome disease activity index (ESSDAI), certain extraglandular manifestations and associated autoimmune conditions (arthropathy, nephropathy, skin and lung manifestations, cryoglobulinemia, vasculitis, systemic lupus erythematosus, rheumatoid arthritis, antiphospholipid syndrome, autoimmune thyroiditis, Raynaud syndrome) and treatment modalities were compared.

2.2 Measurement of routine laboratory parameters

Peripheral blood samples were collected into Vacuette® tubes (Greiner Bio-One Hungary Kft., Mosonmagyaróvár, Hungary). After a half hour rest, tubes were centrifuged at 3500 g 15 min 4 °C and serum/plasma samples were collected. Routine laboratory parameters were measured immediately from fresh samples, while a 500 µl serum aliquot from each patient was stored at -80 °C for subsequent chemerin and oxLDL measurements.

Routine laboratory parameters, including aspartate transaminase (AST), alanine transaminase (ALT), gamma glutamyl transferase (GGT), alkaline phosphatase (AP), lactate dehydrogenase (LDH), estimated glomerular filtration rate (eGFR), urea, creatinine, hematological parameters (leukocyte count, proportion of lymphocytes, neutrophil granulocytes, hemoglobin levels, platelet counts), triglyceride, total cholesterol, low-density lipoprotein-cholesterol [LDL-C], high-density lipoprotein-cholesterol [HDL-C]) were performed according to the standard laboratory methods with a Cobas c600 autoanalyzer (Roche Ltd., Mannheim, Germany) at the Department of Laboratory Medicine, Faculty of Medicine, University of Debrecen, Hungary. Erythrocyte sedimentation rate (ESR), and immune serological markers (presence of anti-Ro/SS-A, anti-La/SS-B, rheumatoid factor, serum immunoglobulin (Ig)A, IgG, IgM and complement levels (c3, c4, 50% hemolytic complement activity (CH50)) were also assessed. All reagents were purchased from the same vendor.

2.3 Measurement of chemerin

Serum chemerin concentrations were measured by a commercially available enzyme linked immunosorbent assay (ELISA) kit (Human Chemerin Quantikine ELISA; Cat.No: DCHM00; R&D Systems, Abingdon, UK), according to the recommendations of the manufacturer. The intra- and inter assay variation coefficients were 2.8-4.5% and 6.4-7.9%, respectively. Samples were used in 100-fold dilution and values were expressed as ng/mL.

2.4 Measurement of oxLDL

Serum concentrations of oxLDL were measured using ELISA (Mercodia AB, Uppsala, Sweden; Cat.No. 10-1143-01). This assay utilizes a direct sandwich technique where two monoclonal antibodies target distinct antigenic determinants on the oxidized apolipoprotein B molecule. The intra-assay and inter-assay CVs were 5.5-7.3% and 4.0-6.2%, respectively. Samples were used in 6561-fold dilution and values were expressed as U/L.

2.5 Statistical analysis

Statistical analyses were performed using the Statistica 13.5.0.17 software (TIBCO Software Inc., Tulsa, OK, USA). GraphPad Prism 8.01 (GraphPad Prism Software Inc., San Diego, CA, USA) was applied to create graphs in the text. Normality of continuous data was tested with the Kolmogorov–Smirnov test. Data were expressed as means $\pm$ SD or medians (interquartile range). Chi-square test was used to analyze categorical data by comparing observed frequencies with expected frequencies. Pearson correlation was used to investigate the relationship between selected variables. Backward stepwise multiple regression analyses were performed to determine significant variables predicted chemerin in overall (Model 1), normal-weight (Model 2) and overweight/obese Sjögren's population (Model 3), respectively. Models were adjusted for BMI, gender, age at the time of Sjögren's diagnosis, statin use and included all variables that correlated with chemerin in the univariate analyses, i.e. c3, c4, log10hsCRP, oxLDL, platelet count and leukocyte count. Variance inflation factors (VIFs) were calculated in each model to characterize collinearity among the predictors. All VIF values were <5 , indicating that multicollinearity was not a concern. $P \leq 0.05$ probability values were considered statistically significant.

3 Results

3.1 Chemerin, oxLDL and ESSDAI

Considering chemerin and oxLDL levels in the non-obese and overweight/obese groups, respectively, there was no significant difference between the two subsets. However, ESSDAI was significantly lower in overweight/obese. (Table 1) No significant difference was found between patients with and without statin therapy regarding chemerin and oxLDL levels.

3.2 Immunological parameters

Regarding immunological parameters, there was no remarkable difference in complement activity (CH50), aSS-A, aSS-B positivity, although c3 and c4 levels were significantly higher in the overweight/obese group. Additionally, the neutrophil granulocyte ratio of overweight/obese patients was significantly lower than in the non-obese group. Regarding immunoglobulins (IgA, IgG, IgM), there was no significant difference between the two groups. (Table 2).

3.3 Routine laboratory parameters and medications

As for liver function tests, gamma-glutamyl transferase (GGT and alanine transaminase (ALT)) levels of non-obese patients were significantly lower. Hemoglobin and hematocrit were significantly higher in overweight/obese patients. Cholesterol levels of the overweight/obese group were lower; however, triglyceride levels were significantly higher (Table 3). Also, not surprisingly, in the overweight/obese category, statin therapy was administered significantly more frequently (18,52% vs. 41,67%; $p=0.04$).

TABLE 1 Differences in body mass index, chemerin and oxLDL levels and EULAR disease activity index (ESSDAI) between the two groups (1: non-obese, 2: overweight/obese).

Variables	Non-obese (mean $\pm$ SD)	Overweight/ obese (mean $\pm$ SD)	F-ratio variances	p
BMI	22.41 $\pm$ 2.24	31.06 $\pm$ 4.40	3.86	<0.0001
Chemerin (ng/ml)	96.43 $\pm$ 20.10	106.03 $\pm$ 25.88	1.66	0.17
oxLDL (U/L)	98.03 $\pm$ 31.23	107.81 $\pm$ 37.99	1.48	0.29
ESSDAI	5.04 $\pm$ 4.26	2.76 $\pm$ 2.92	2.13	0.04

Bold values indicate statistically significant results in the tables.

TABLE 2 Relevant immunological parameters of the two groups (1: non-obese, 2: overweight/obese).

Variables	Non-obese (mean $\pm$ SD)	Overweight/ obese (mean $\pm$ SD)	F-ratio variances	p
Lymphocyte ratio (%)	21.86 $\pm$ 9.72	29.06 $\pm$ 9.26	1.10	0.75
Neutrophil ratio (%)	66.95 $\pm$ 11.64	58.59 $\pm$ 10.43	1.25	0.002
c3 (g/l)	1.20 $\pm$ 0.19	1.46 $\pm$ 0.52	6.96	<0.001
c4 (g/l)	0.20 $\pm$ 0.08	0.27 $\pm$ 0.09	1.57	0.003
CH50	68.34 $\pm$ 18.58	70.67 $\pm$ 14.66	1.60	0.16
aSS-A positivity	0.63 $\pm$ 0.49	0.48 $\pm$ 0.50	1.05	0.21
aSS-B positivity	0.48 $\pm$ 0.51	0.29 $\pm$ 0.46	1.21	0.12
IgA (g/l)	2.31 $\pm$ 1.33	2.29 $\pm$ 1.40	1.10	0.97
IgG (g/l)	12.86 $\pm$ 7.25	10.66 $\pm$ 6.76	1.15	0.19
IgM (g/l)	1.99 $\pm$ 2.67	2.10 $\pm$ 3.28	1.49	0.88

Bold values indicate statistically significant results in the tables.

TABLE 3 Relevant routine laboratory parameters of the two groups (1: non-obese, 2: overweight/obese).

Variables	Non-obese (mean $\pm$ SD)	Overweight/ obese (mean $\pm$ SD)	Std. dev. 1	Std. dev. 2	F-ratio variances	p
GGT (U/L)	26.70 $\pm$ 25.26	48.23 $\pm$ 58.23	25.26	58.23	5.32	<0.001
ALT (U/L)	21.67 $\pm$ 17.82	29.13 $\pm$ 31.78	17.82	31.78	3.18	0.002
Hemoglobin (g/l)	126.15 $\pm$ 14.69	133.48 $\pm$ 10.59	14.69	10.59	1.92	0.014
Hematocrit	0.38 $\pm$ 0.042	0.39 $\pm$ 0.03	0.042	0.03	2.38	0.01
Platelet count (G/L)	263.74 $\pm$ 75.33	244.69 $\pm$ 64.88	75.33	64.88	1.35	0.25
Cholesterol (mmol/L)	5.05 $\pm$ 1.22	4.95 $\pm$ 1.24	1.22	1.24	1.03	0.73
Triglyceride (mmol/L)	1.15 $\pm$ 0.48	1.58 $\pm$ 0.65	0.48	0.65	1.81	0.004

Bold values indicate statistically significant results in the tables.

3.4 Correlations with chemerin and oxLDL levels

Since comparative tests did not reveal considerable results concerning adipokines, we also examined the correlation of certain parameters with chemerin and oxLDL levels of all our patients, without categorizing them. A significant positive correlation was found between serum chemerin level and BMI (Figure 1A), age at diagnosis (Figure 1B), c3 (Figure 2A), c4 (Figure 2B), C-reactive Protein (CRP) (Figure 2C), platelet count (Figure 3A) and leukocyte count (Figure 3B). Examining the correlation of ESSDAI, a negative correlation was found with serum chemerin levels, however, it was

not significant ($r=-0.073$, $p=0.578$). In case of oxLDL, we found significant positive correlations with cholesterol levels ($r=0.626$, $p<0.001$), and with leukocyte count ($r=0.276$, $p=0.017$). Regarding further laboratory parameters (e.g. kidney function, liver enzymes, autoantibodies), correlation results were not significant.

3.5 Platelet-associated inflammatory signaling as a determinant of chemerin levels

Backward stepwise multiple regression analyses were performed to determine significant predictor(s) of chemerin levels in overall,

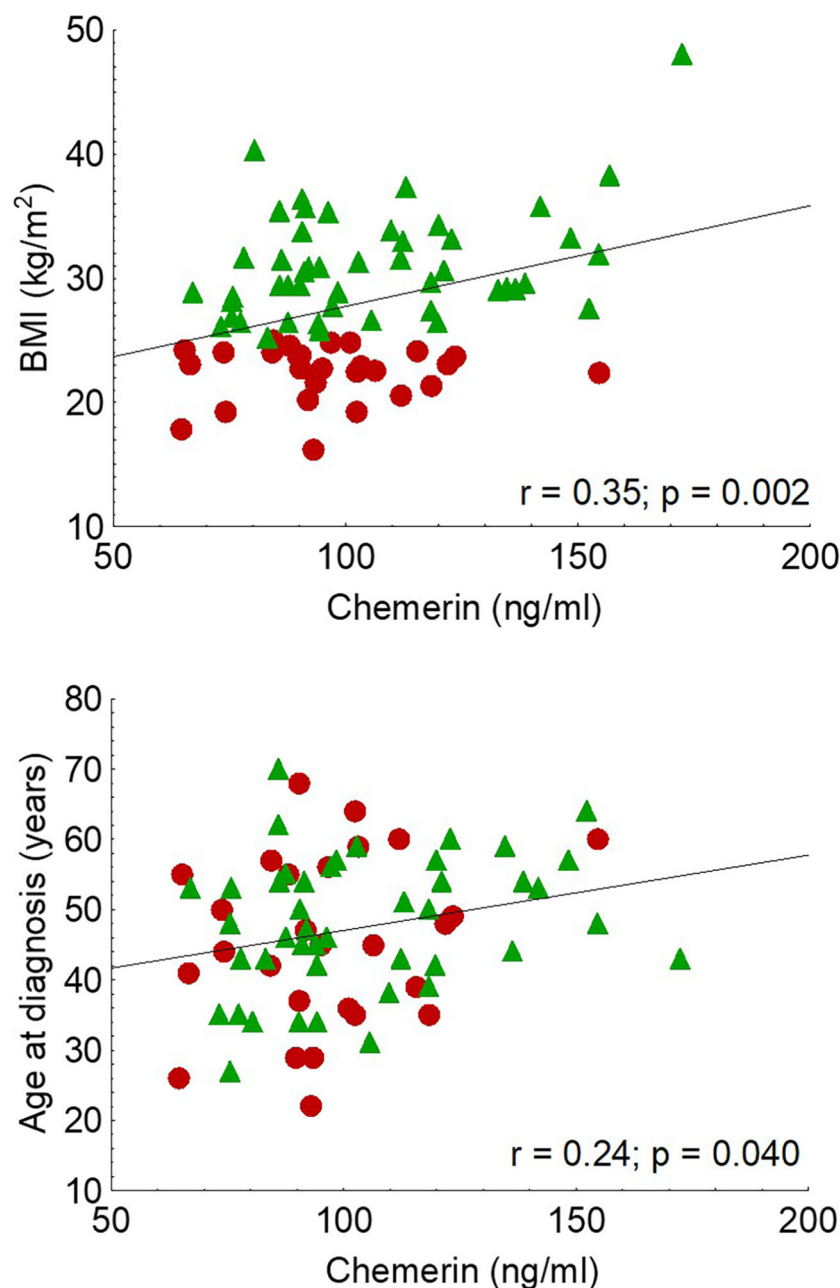


FIGURE 1

Correlation between BMI and chemerin levels (green: overweight/obese, red: non-obese). Correlation between age at diagnosis and chemerin levels (green: overweight/obese, red: non-obese).

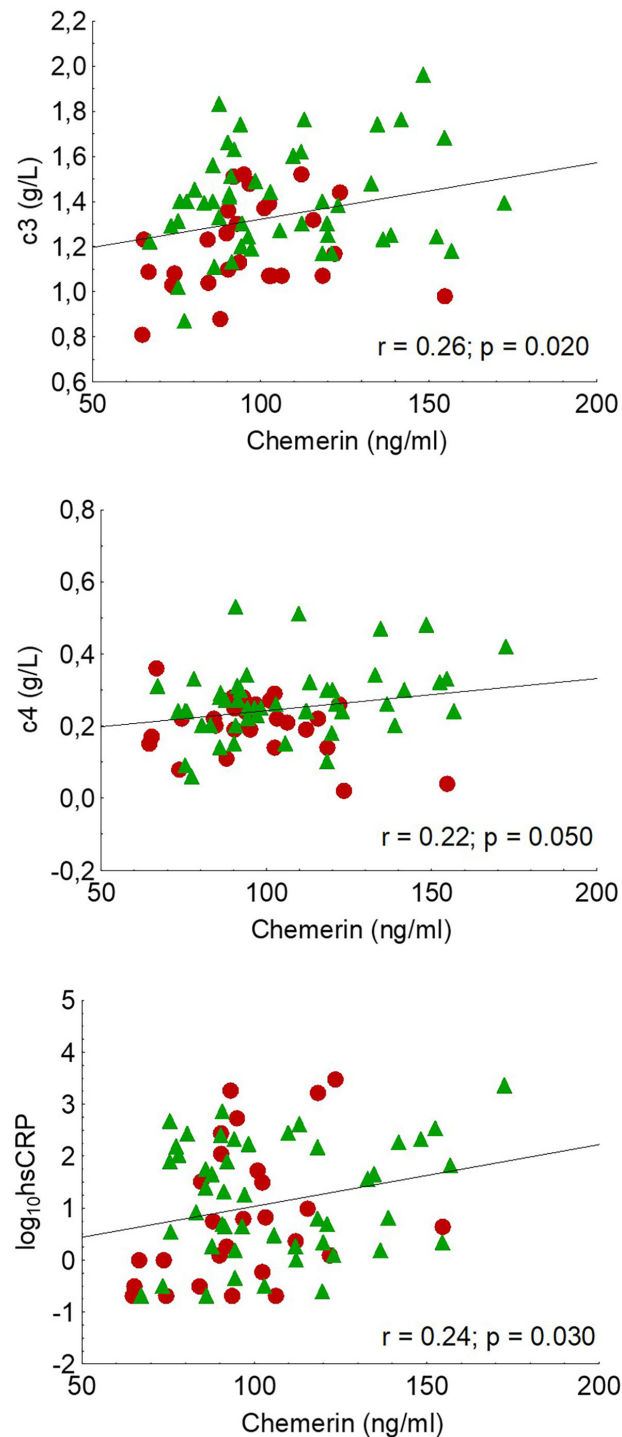


FIGURE 2

Correlation between c3 and chemerin levels (green: overweight/obese, red: non-obese). Correlation between c4 and chemerin levels (green: overweight/obese, red: non-obese). Correlation between CRP and chemerin levels (green: overweight/obese, red: non-obese).

normal-weight and overweight/obese Sjögren's disease cohort. Models were adjusted for BMI, gender, and age at the time of Sjögren's diagnosis, and included all variables that correlated with chemerin in the univariate analyses (Table 4). In overall and in the obese group, BMI (overall: $\beta_{\text{standardized}}=0.364$; $P<0.001$ and

overweight/obese: $\beta_{\text{standardized}}=0.335$; $P<0.001$) and platelet count (overall: $\beta_{\text{standardized}}=0.524$; $P<0.001$ and overweight/obese: $\beta_{\text{standardized}}=0.456$; $P = 0.001$) were independent predictors of chemerin. In normal-weight Sjögren's patients, platelet count was a predictor of chemerin ($\beta_{\text{standardized}}=0.0647$; $P = 0.001$).

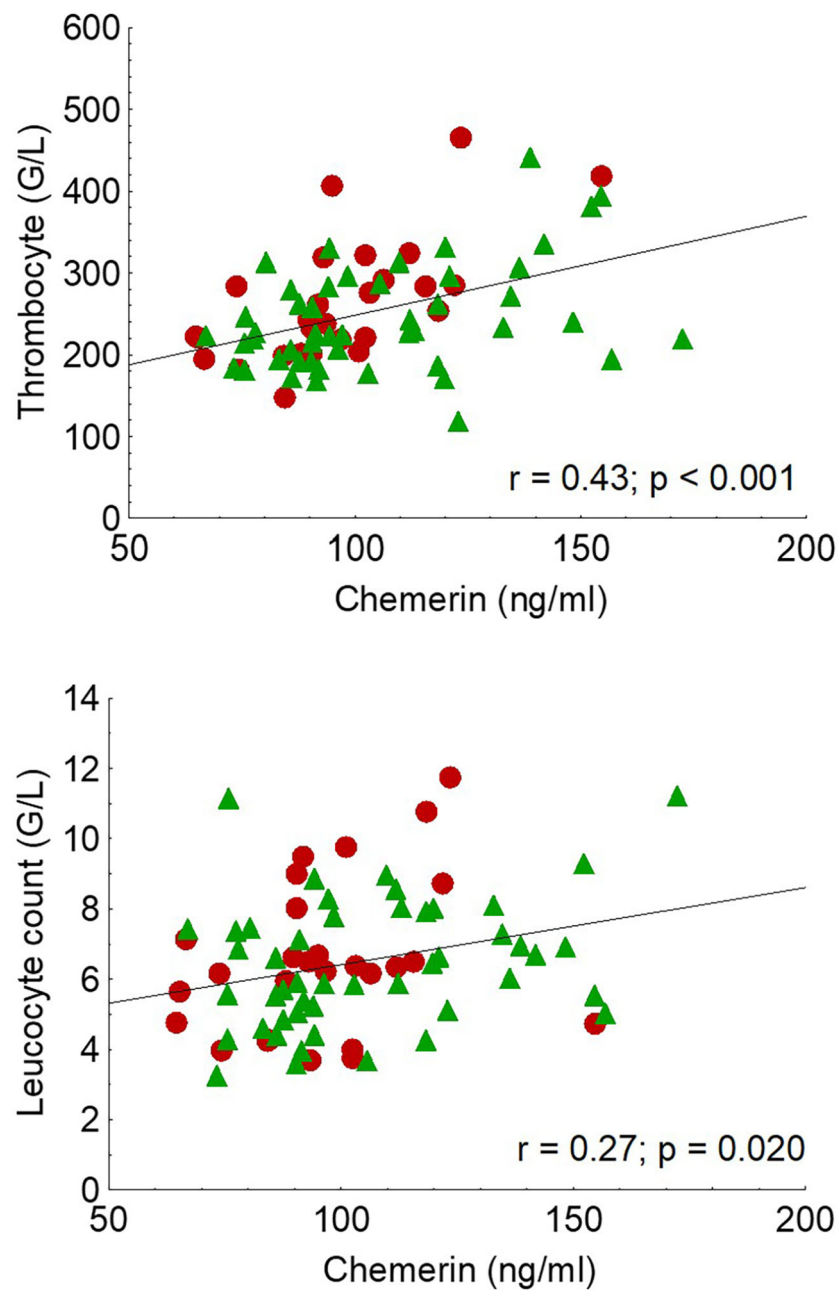


FIGURE 3

Correlation between platelet count and chemerin levels (green: overweight/obese, red: non-obese). Correlation between Leucocyte count and chemerin levels (green: overweight/obese, red: non-obese).

TABLE 4 Backward stepwise multiple regression analyses to determine significant variables predicted chemerin in overall, overweight/obese and normal-weight Sjögren cohort.

Variable	Overall		Overweight/obese		Non-obese	
	$\beta_{\text{standardized}}$	P-value	$\beta_{\text{standardized}}$	P-value	$\beta_{\text{standardized}}$	P-value
BMI (kg/m ²)	0.364	<0.001	0.335	0.012	0.181	0.248
Gender (m/f)	-0.073	0.455	-0.070	0.613	-0.174	0.269
Age at diagnosis (years)	0.137	0.164	0.110	0.429	0.098	0.610
Statin use (yes/no)	-0.043	0.670	-0.118	0.385	0.151	0.413

(Continued)

TABLE 4 Continued

Variable	Overall		Overweight/ obese		Non-obese	
	$\beta_{\text{standardized}}$	P-value	$\beta_{\text{standardized}}$	P-value	$\beta_{\text{standardized}}$	P-value
c3 (g/L)	0.041	0.748	0.160	0.226	-0.240	0.275
c4 (g/L)	0.138	0.192	0.111	0.522	0.184	0.377
log10hsCRP	-0.032	0.785	-0.124	0.402	0.144	0.424
oxLDL (U/L)	0.051	0.613	0.128	0.343	-0.219	0.295
Platelet count (G/L)	0.523	<0.001	0.456	0.002	0.647	<0.001
Leukocyte count (G/L)	0.073	0.481	0.115	0.416	0.044	0.845

Bold values indicate statistically significant results in the tables.

4 Discussion

According to our results, several parameters seem to be more favourable in overweight/obese patients, even the disease activity index (ESSDAI) is significantly lower than the patients with normal body weight.

Based on currently available academic information, we expected chemerin and oxLDL levels to be higher in the overweight/obese group, given their established associations with adipose tissue and metabolic dysfunction. However, regarding our patients, there was no significant difference between the two groups. Chemerin is also stated to be a pro-inflammatory adipokine, therefore, less beneficial parameters of the overweight/obese group were expected. The absence of a significant difference between the groups therefore suggests that the relationship between adiposity and circulating chemerin may be more complex in Sjögren's disease.

In our cohort, mean chemerin levels in the overweight/obese group were lower, compared to results of several other available studies (36–39). Of course, having other types of kits used to determine chemerin levels could be one of the reasons behind this finding, but revising available data, there was no remarkable difference between results determined by different kits. However, we admit the limitations of our study, since it did not include a healthy control group and the difference between the overweight/obese and non-obese Sjögren's groups was not statistically significant. The relatively lower chemerin concentrations observed in our overweight/obese patients may represent a potential hypothesis linking adipokine signaling with the lower ESSDAI observed in this group, but this possibility requires confirmation in larger, controlled and prospective studies.

As stated previously, chemerin plays an important role in the inflammatory process, mediating pathways and sustaining inflammation. According to several studies, chemerin is being researched as a potential biomarker for immunity and chronic diseases, as its elevated level could indicate the risk or severity of certain illnesses. Its biomarker aspect is already being researched in metabolic diseases, systemic lupus erythematosus, psoriasis vulgaris and rheumatoid arthritis. In psoriasis patients, a higher level of chemerin was found compared to healthy individuals and its level also correlated positively with the disease severity index. In Rheumatoid arthritis, high level of

chemerin indicated higher clinical disease activity, more pronounced joint involvement and higher inflammatory marker levels (37, 39, 40). Considering these results, since chemerin levels of our overweight/obese patients were lower than expected, it is quite logical that their disease activity score indicates a less severe disease burden. In systemic lupus erythematosus, it did not prove to be a good marker of severity, however, a relevance was found between chemerin levels and specific organ involvements, such as lupus nephritis, as its circulating levels were found to correlate with kidney function in some studies (41).

One of the most notable findings of our study was the independent association between platelet count and circulating chemerin levels. Beyond their traditional role in hemostasis, platelets are increasingly recognized as active mediators of innate immunity and chronic inflammatory responses. Platelet activation contributes to endothelial dysfunction, leukocyte recruitment, cytokine release, and thromboinflammatory signaling, all of which are involved in autoimmune-mediated vascular injury and accelerated atherosclerosis. In autoimmune rheumatic diseases, elevated platelet count and platelet activation have already been associated with systemic inflammatory burden and vascular complications. Since chemerin also participates in inflammatory cell recruitment, adipose tissue signaling, and endothelial inflammatory pathways, the observed correlation may reflect a shared immunometabolic-inflammatory axis in Sjögren's disease. This relationship could partly explain the link between systemic inflammation, adipokine dysregulation, and increased cardiovascular risk observed in these patients (42–44). Interestingly, platelet count remained an independent predictor of chemerin levels even after adjustment for BMI and demographic variables. This finding suggests that circulating chemerin concentrations may be influenced not only by adipose tissue mass but also by inflammatory and hematologic mechanisms. Considering the recognized role of platelets in endothelial activation and atherogenesis, platelet-associated inflammatory signaling may represent an additional pathway contributing to vascular dysfunction in Sjögren's disease. Therefore, chemerin may represent a potential molecular interface between adipose tissue dysfunction, innate immune activation, and vascular inflammation in Sjögren's disease.

As discussed in our previous paper, the significance of statin therapy must be emphasized. The substantially higher prevalence of

statin therapy in the overweight/obese cohort represents a potentially important contributing factor. Given the pleiotropic anti-inflammatory effects of statins and their emerging interactions with adipokine signaling, part of the observed reduction in disease activity may reflect pharmacologic, rather than obesity-related immunomodulation, since it helps to reduce inflammation by interacting with pathways involving Rho/Rac signaling, NF- κ B activation, elevating nitric oxide levels and lowering CRP level while also having immunomodulatory features (16–20). Statins can interfere with chemerin levels, however there is very limited available academic information about this, although, it could be explained by their anti-inflammatory effect. Some studies state that they can lower circulating chemerin levels by more than 30%, while PCSK-9 inhibitors did not seem to have any effect, making this a unique feature of statins (45).

Although oxLDL levels did not differ significantly between groups, platelet-associated inflammatory signaling appeared more strongly linked to chemerin levels, suggesting that cellular inflammatory pathways may be more relevant than circulating oxidized lipid burden in this cohort.

We acknowledge several limitations of our study. The relatively small sample size and single-center design may limit the statistical power and generalizability of our findings. Given that this was a cross-sectional study, causal relationships between adiposity, chemerin levels, inflammatory parameters, statin use, and disease activity cannot be established. Also, no healthy control group was included. Furthermore, our study was based primarily on clinically available data, and detailed lipid fractions and other potentially relevant metabolic and inflammatory parameters were not systematically assessed. The higher prevalence of statin therapy in the overweight/obese group represents an additional potential confounding factor, as statins may influence inflammatory and immunometabolic pathways, including chemerin signaling. Therefore, the observed differences between BMI groups cannot be attributed to adiposity alone. Finally, the available clinical literature on adipokines in autoimmune diseases remains relatively limited, making direct comparison and interpretation of our findings challenging. Larger, multicenter, controlled and prospective studies are warranted to validate these findings and further clarify the role of adipokines and platelet-associated inflammatory pathways in Sjögren's disease. Nevertheless, adipokines represent a promising area of research, and we hope to further investigate their role and facilitate their integration into routine clinical practice.

5 Conclusions

In summary, our results suggest that overweight/obese patients with Sjögren's disease may exhibit lower measured systemic disease activity despite the well-established adverse cardiovascular consequences associated with excess body weight. Distinct immune-

metabolic and platelet-associated inflammatory pathways may contribute to disease activity and vascular risk in Sjögren's disease. The greater use of statins among obese patients raises the possibility that statin-associated anti-inflammatory and immunometabolic effects may contribute to the observed differences, although this cannot be established in our cross-sectional study. Prospective studies should be carried out to investigate whether statin therapy influences chemerin levels, systemic inflammation, and disease activity in Sjögren's disease. BMI and platelet count were independently associated with chemerin levels.

Nevertheless, this is the first paper assessing chemerin levels in patients with Sjögren's disease.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Regional and Institutional Research Ethics Committee. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

KM: Formal analysis, Methodology, Investigation, Writing – original draft, Conceptualization. VO: Validation, Writing – review & editing. IH: Writing – review & editing, Resources. ZA: Writing – review & editing, Validation. HL: Visualization, Data curation, Formal analysis, Project administration, Writing – review & editing, Methodology, Software, Investigation. MH: Methodology, Investigation, Writing – review & editing. AS: Investigation, Writing – review & editing, Methodology, Conceptualization, Supervision, Resources.

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Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

- Baldini C, Fulvio G, La Rocca G, Ferro F. Update on the pathophysiology and treatment of primary Sjögren syndrome. *Nat Rev Rheumatol*. (2024) 20:473–91. doi: 10.1038/s41584-024-01135-3
- Negrini S, Emmi G, Greco M, Borro M, Sardaneli F, Murdaca G, et al. Sjögren's syndrome: a systemic autoimmune disease. *Clin Exp Med*. (2022) 22:9–25. doi: 10.1007/s10238-021-00728-6
- Jonsson R. Disease mechanisms in Sjögren's syndrome: what do we know? *Scand J Immunol*. (2022) 95:e13145. doi: 10.1111/sji.13145
- Karakasis P, Patoulas D, Stachteas P, Lefkou E, Dimitroulas T, Fragakis N. Accelerated atherosclerosis and management of cardiovascular risk in autoimmune rheumatic diseases: an updated review. *Curr Probl Cardiol*. (2023) 48:101999. doi: 10.1016/j.cpcardiol.2023.101999
- Luczak A, Malecki R, Kulus M, Madej M, Szahidewicz-Krupska E, Doroszko A. Cardiovascular risk and endothelial dysfunction in primary Sjögren syndrome is related to the disease activity. *Nutrients*. (2021) 13:2072. doi: 10.3390/nu13062072
- Mortensen MB, Jensen JM, Ronnow Sand NP, Kragholm K, Blaha MJ, Grove EL, et al. Association of autoimmune diseases with coronary atherosclerosis severity and ischemic events. *J Am Coll Cardiol*. (2024) 83:2643–54. doi: 10.1016/j.jacc.2024.04.030
- Bacon PA, Stevens RJ, Carruthers DM, Young SP, Kitas GD. Accelerated atherogenesis in autoimmune rheumatic diseases. *Autoimmun Rev*. (2002) 1:338–47. doi: 10.1016/S1568-9972(02)00100-3
- Hildebrand S, Pfeifer A. The obesity pandemic and its impact on non-communicable disease burden. *Pflugers Arch - Eur J Physiol*. (2025) 477:657–68. doi: 10.1007/s00424-025-03066-8
- Mousavi S, Bieber K, Zirpel H, Vorobyev A, Olbrich H, Papara C, et al. Large-scale analysis highlights obesity as a risk factor for chronic, non-communicable inflammatory diseases. *Front Endocrinol*. (2025) 16:1516433. doi: 10.3389/fendo.2025.1516433
- Australian Institute of Health and Welfare. *Living With Overweight or Obesity Overtakes Tobacco as New Leading Burden of Disease Risk Factor: Australian Burden of Disease Study 2024*. Canberra, Australia: Australian Institute of Health and Welfare (2024).
- Mezei K, Nagy L, Orosz V, Aradi Z, Bói B, Szántó A. Obesity: friend or foe in Sjögren's syndrome patients? *Diagnostics*. (2024) 14:2725. doi: 10.3390/diagnostics14232725
- Curtis JP, Selter JG, Wang Y, Rathore SS, Jovin I, Jadbabaie F, et al. The obesity paradox: body mass index and outcomes in patients with heart failure. *Arch Intern Med*. (2005) 165:55–61. doi: 10.1001/archinte.165.1.55
- Hou C, Qi Y, Zhang T, Liu Y, Wu J, Li W, et al. Evaluating the obesity paradox in patients with sepsis and cancer. *Int J Obes*. (2025) 49:1723–32. doi: 10.1038/s41366-025-01805-6
- Chen Q-F, Ni C, Katsouras CS, Liu C, Yao H, Lian L, et al. Obesity paradox in patients with acute coronary syndrome: is malnutrition the answer? *Nutr Dis*. (2024) 165(1):55–61. doi: 10.1016/j.tjnut.2024.04.016
- Khan S, Huda B, Bhurka F, Patnaik R, Banerjee Y. Molecular and immunomodulatory mechanisms of statins in inflammation and cancer therapeutics with emphasis on the NF- κ B, NLRP3 inflammasome, and cytokine regulatory axes. *Int J Mol Sci*. (2025) 26:8429. doi: 10.3390/ijms26178429
- Kim S-K, Choe J-Y, Kim J-W, Park K-Y. HMG-CoA reductase inhibitors suppress monosodium urate-induced NLRP3 inflammasome activation through PPAR- γ activation in THP-1 cells. *Pharmaceutics*. (2025) 16:522. doi: 10.3390/ph16040522
- Koushki K, Shahbaz SK, Mashayekhi K, Sadeghi M, Zayeri ZD, Taba MY, et al. Anti-inflammatory action of statins in cardiovascular disease: the role of inflammasome and toll-like receptor pathways. *Clin Rev Allergy Immunol* (2021) 60 (2):175–199. doi: 10.1007/s12016-020-08791-9
- Wang S, Xie X, Lei T, Zhang K, Lai B, Zhang Z, et al. Statins attenuate activation of the NLRP3 inflammasome by oxidized LDL or TNF- α in vascular endothelial cells through a PXR-dependent mechanism. *J Pharmacol Exp Ther*. (2017) 362:411–9. doi: 10.1124/mol.116.108100
- Khattari S, Zandman-Goddard G. Statins and autoimmunity. *Immunol Res*. (2013) 56:348–57. doi: 10.1007/s12026-013-8409-8
- Dehnavi S, Sohrabi N, Sadeghi M, Lansberg P, Banach M, Al-Rasadi K, et al. Statins and autoimmunity: state-of-the-art. *Pharmacol Ther*. (2020) 214:107614. doi: 10.1016/j.pharmthera.2020.107614
- Kotyła PJ, Kucharz EJ. Statins therapy for connective tissue diseases: new therapeutic opportunities. *Endocr Metab Immune Disord Drug Targets*. (2018) 18:135–47. doi: 10.2174/187153031766617116115120
- Pestel J, Blangero F, Watson J, Pirola L, Eljaafari A. Adipokines in obesity and metabolic-related diseases. *Biochimie*. (2023) 212:48–59. doi: 10.1016/j.biochi.2023.04.008
- Kim JE, Kim JS, Jo MJ, Cho E, Ahn SY, Kwon YJ, et al. The roles and associated mechanisms of adipokines in development of metabolic syndrome. *Molecules*. (2022) 27:334. doi: 10.3390/molecules27020334
- Taylor EB. The complex role of adipokines in obesity, inflammation, and autoimmunity. *Clin Sci*. (2021) 135:731–52. doi: 10.1042/cs20200895
- Mariowska A, Horwat P, Szymańska A, Pierdzka W, Dzieciatkowska M. The impact of obesity on the development and progression of selected autoimmune diseases: interplay between inflammation and immune dysregulation—focus on adipokines. *Med Sci*. (2025) 29:e191ms3646. doi: 10.54905/diss.v29i163.e191ms3646
- Laffranchi M, Schioppa T, Sozio F, Piserà A, Tiberio L, Salvi V, et al. Chemerin in immunity. *J Leukoc Biol*. (2025) 117:qiae181. doi: 10.1093/leuko/qiae181
- Su X, Cheng Y, Zhang G, Wang B. Chemerin in inflammatory diseases. *Clin Chim Acta*. (2021) 517:41–7. doi: 10.1016/j.cca.2021.02.010
- Sun JX, Zhang C, Cheng ZB, Tang MY, Liu YZ, Jiang JF, et al. Chemerin in atherosclerosis. *Clin Chim Acta*. (2021) 520:8–15. doi: 10.1016/j.cca.2021.05.015
- Yu M, Yang Y, Huang C, Ge L, Xue L, Xiao Z, et al. Chemerin: a functional adipokine in reproductive health and diseases. *Biomedicine*. (2022) 10:1910. doi: 10.3390/biomedicine10081910
- Tarantino G, Citro V. Liver-spleen axis: Deciphering a crucial crosstalk in non-alcoholic fatty liver disease progression and therapeutic implications. *World J Gastroenterol*. (2026) 32:119467. doi: 10.3748/wjg.119467
- Zhang J, Chang J, Chen V, Beg MA, Huang W, Vick L, et al. Oxidized LDL stimulates PKM2-mediated mtROS production and phagocytosis. *J Lipid Res*. (2025) 66:100809. doi: 10.1016/j.jlr.2025.100809
- Mosalmanzadeh N, Pence BD. Oxidized low-density lipoprotein and its role in immunometabolism. *Int J Mol Sci*. (2024) 25:11386. doi: 10.3390/ijms252111386
- Zhevlakova I, Liu H, Dudiki T, Gao D, Yakubenko V, Tkachenko S, et al. Mechanisms and consequences of myeloid adhesion dysfunction in atherogenesis. *Cardiovasc Res*. (2025) 121:62–76. doi: 10.1093/cvr/cvae223

34. Gliozzi M, Scicchitano M, Bosco F, Musolino V, Carresi C, Scarano F, et al. Modulation of nitric oxide synthases by oxidized LDLs: role in vascular inflammation and atherosclerosis development. *Int J Mol Sci.* (2019) 20:3294. doi: 10.3390/ijms20133294
35. Zingg JM, Vlad A, Ricciarelli R. Oxidized LDLs as signaling molecules. *Antioxidants.* (2021) 10:1184. doi: 10.3390/antiox10081184
36. Sell H, Divoux A, Poitou C, Basdevant A, Bouillot JL, Bedossa P, et al. Chemerin correlates with markers for fatty liver in morbidly obese patients and decreases after weight loss induced by bariatric surgery. *J Clin Endocrinol Metab.* (2010) 95:2892–6. doi: 10.1210/jc.2009-2374
37. Gonzalez-Ponce F, Gamez-Nava JL, Perez-Guerrero EE, Saldaña-Cruz AM, Vazquez-Villegas ML, Ponce-Guarneros JM, et al. Serum chemerin levels: a potential biomarker of joint inflammation in women with rheumatoid arthritis. *PLoS One.* (2021) 16:e0255854. doi: 10.1371/journal.pone.0255854
38. Li Y, Shi B, Li S. Association between serum chemerin concentrations and clinical indices in obesity or metabolic syndrome: a meta-analysis. *PLoS One.* (2014) 9:e113915. doi: 10.1371/journal.pone.0113915
39. Eichelmann F, Weikert C, Di Giuseppe R, Biemann R, Isermann B, Schulze MB, et al. Methodological utility of chemerin as a novel biomarker of immunity and metabolism. *Endocr Connect.* (2017) 6:340–7. doi: 10.1530/ec-17-0098
40. Imam M, Ghonemy S, Elsayed H, Osama Z, Anis N. Chemerin: an adipokine involved in pathogenesis and severity of psoriasis vulgaris. *Zagazig Univ Med J.* (2025) 31:938–44. doi: 10.21608/zumj.2025.350048.3776
41. Corona-Meraz FI, Vázquez-Del Mercado M, Sandoval-García F, Robles-De Anda JA, Tovar-Cuevas AJ, Rosales-Gómez RC, et al. Biomarkers in systemic lupus erythematosus along with metabolic syndrome. *J Clin Med.* (2024) 13:1988. doi: 10.3390/jcm13071988
42. Jakubaszek M, Kwiatkowska B, Plaza M, Maślińska M. Platelet count correlates with systemic inflammation but not with synovial vascularity in rheumatoid and psoriatic arthritis: a cross-sectional ultrasound-based study. *Rheumatol Int.* (2026) 46(1):4. doi: 10.1007/s00296-025-06047-3
43. Matwiejuk M, Kulczyńska-Przybik A, Łukaszuk B, Myśliwiec H, Myśliwiec P, Chabowski A, et al. Evaluation of chemerin levels in the pathogenesis of psoriasis. *Front Med.* (2026) 13:1748469. doi: 10.3389/fmed.2026.1748469
44. Kaser A, Brandacher G, Steurer W, Kaser S, Offner FA, Zoller H, et al. Interleukin-6 stimulates thrombopoiesis through thrombopoietin: role in inflammatory thrombocytosis. *Blood.* (2001) 98:2720–5. doi: 10.1182/blood.v98.9.2720
45. Tan L, Wang N, Galema-Boers AMH, van Vark-van der Zee L, van Lennep JR, Mulder MT, et al. Statins, but not proprotein convertase subtilisin-kexin type 9 inhibitors, lower chemerin in hypercholesterolemia via low-density lipoprotein receptor upregulation. *MedComm.* (2024) 5:e681. doi: 10.1002/mco2.681