

# Poster Round

## 海報目錄

時間：112年11月26日(星期日)14:35-14:50

地點：台南遠東香格里拉飯店 B2 海報區

主持人：蘇昱日醫師

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**The safety of COVID-19 vaccinations in patients with allergic, immunologic, and rheumatic diseases: a multiple center study in Northern and Eastern Taiwan**

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Patients with allergic, immunologic, and rheumatic disease have potential are vulnerable to the global pandemic of COVID-19 since the winter in 2019. Some patients still hesitated about vaccinations which had Emergency Use Authorization in Taiwan, due to the risk of vaccine-triggered inflammation, vaccine-induced thrombotic thrombocytopenia by adenovirus-vector vaccines, and myocarditis related to mRNA-based vaccines. This large-scale study accumulated a detailed safety profile for patients with autoimmune rheumatic diseases. A total of 3631 patients receiving 7848 doses of COVID-19 vaccines were enrolled in this study. There were 2440 patients completed 2 doses, 1486 patients received total 3 doses, 261 received 4 doses, and 30 patients received 5 doses of vaccines. The most common vaccine brands were Moderna (including next generations) 3791 doses, AZ 2157 doses, Pfizer/BNT 1536 doses, and MVC 284 doses. Among all doses of vaccines, the most common side effect were local pain (54.49%), fatigue or lethargy (23.19%), myalgia (16.99%), headache (12.77%), arthralgia (10.19%), low-grade fever (9.11%), high fever (7.54%), generalized pain (6.49%), and local erythema (6.1). The risk of daily life impairment or requirement of a vacation from work were 172 person times (2.19%). The risk of vaccine-induced emergency care or hospitalization was 69 person times (0.88%). This evidence advocated that patients allergic, immunologic, and rheumatic diseases are generally tolerable to COVID-19 vaccines in Taiwan. Most of the side effects were self-limited and controllable. To avoid severe COVID-19 infection and death, patients are suggested to received COVID-19 vaccines if their disease activity are stable.

## RNA Immunoprecipitation, ICAP ANA Pattern and Line Immunoblot assay for Detecting Anti-SRP Antibodies in Patients with Myopathy

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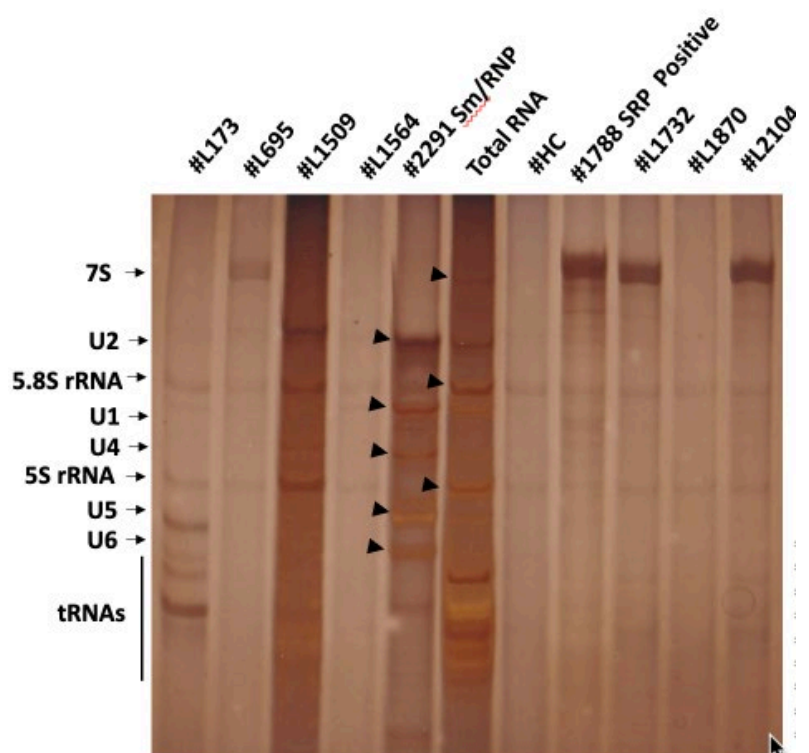
**Background:** Anti-signal recognition particle (SRP) antibodies in patients with myopathy using RNA immunoprecipitation (RNA-IP) for 7S RNA is a gold standard. The ICAP ANA pattern of anti-SRP antibody was not well recognized. The performance of Euroimmune line immunoblot assay for anti-SRP antibody in Taiwanese was not reported.

**Methods:** RNA-IP was performed to detect anti-SRP antibodies in 43 patients positive for anti-SRP antibodies by line immunoblot assay from 2021 Jan to 2023 June. The ICAP ANA pattern was recorded for each patient. And the clinical features of interstitial lung diseases and CPK values were recorded. The incidence of interstitial lung disease was determined by lung HRCT.

**Results:** Among 43 Line immunoblot anti-SRP antibody-positive patients, 25 patient was positive for 7SRNA by RNA-IP (Fig 1) and 18 patient was negative for 7S RNA, i.e. false positive anti-SRP antibody. The high false positive rate should be noted in real-world practice. All the 7S RNA-positive patients showed AC-19 ICAP ANA pattern. Among the real Anti-SRP antibody positive patients, all patients showed high CPK >1000 U/L. The Interstitial lung disease was documented by HRCT in 9/25 (36%).

**Conclusion:** 7S RNA by RNA-IP is a gold standard for detecting anti-SRP antibody. All anti-SRP antibody positive patients showed a ICAP AC-19 pattern. Euroimmune line blot detection of anti-SRP antibody may show high false positive rate.

Figure 1. #1732, #1870, #2104 showed 7SRNA by RNA IP.



**Unmasking the Rods and Rings Antinuclear Antibody Pattern: Not only hepatitis C infection with treatment but also a risk marker of cerebral-cardiovascular disease**

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**Background:**

The rods and rings (RR) antinuclear antibody (ANA) pattern, known as AC-23, is typically associated with hepatitis C treatment. The clinical significance of this pattern, however, remains unexplored. This study probes the link of RR pattern with various clinical conditions.

**Methods:**

A retrospective analysis was conducted on ANA samples from the Chang Gung Memorial Hospital, Linkou, from 2019 to 2021. Positive ANA was defined as a titer of ANA  $\geq$  1:160. ANA patterns, identified using EUROPattern (EUROIMMUN, Germany), were correlated with initial clinical data.

**Results:**

Among 43,633 samples, 22.9% tested positive for ANA. Among these, the RR ANA pattern was exhibited in 55 samples from 35 patients. The patients were predominantly male (n=22), with a mean age of 68 years. Most RR-positive patients (88.6%) showed positive Hepatitis C virus (HCV) serology. Four patients (11.4%), with diseases unrelated to HCV infection, were also found to express this pattern. Notably, three out of these four patients were on beta-blocker therapy. A subsequent comparison between patients with high ( $\geq$  1:640) and low ( $\leq$  1:320) titer ANA revealed a significantly higher frequency of CVD in the high titer Anti-RR pattern ANA group (p=0.026), with no other significant demographic, clinical, or laboratory differences.

**Conclusion:**

Beyond its association with hepatitis C treatment, the RR pattern in ANA may also indicate a risk for CVD, particularly at high titers, highlighting new avenues for research.

## Multidisciplinary approach of hereditary angioedema (HAE) in high-risk patients with unexplained angioedema: preliminary screening in a private hospital system

單一醫療體系以跨團隊方式對遺傳性血管性高風險水腫患者所進行的初步篩檢

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## Background

Hereditary angioedema (HAE) with deficiency of C1 esterase inhibitor (C1 INH) is a rare genetic disorder characterized by recurrent episodes of cutaneous or submucosal edema. HAE diagnosis is frequently delayed or missed in part because of low disease awareness, causing patients to undergo unnecessary procedures and face increased risk of life-threatening laryngeal attacks. Furthermore, the natural course of HAE among Taiwanese patients remains largely obscure and appropriate screening strategies are unavailable.

## Methods

Patients who received care in our private hospital system between June 2022 and March 2023 were screened by the following criteria: (1) unexplained and recurrent angioedema; (2) positive family history of angioedema; (3) recurrent and painful abdominal symptoms; (4) failure to respond to antihistamines, glucocorticoids, or epinephrine; (5) occurrence of upper airway edema; and (6) low C4 level. Individuals meeting the first two criteria and/or the other criteria underwent C1-INH testing using chromogenic assays.

## Results

A total of 98 patients met the screening criteria, of which 2 patients had low C1-INH levels and were

diagnosed with HAE based on clinical presentations and serology results, yielding a hit rate of about 2%. Both patients were successfully treated with icatibant for HAE attack.

### **Conclusion**

HAE is widely underdiagnosed in Taiwan. Given the availability of effective treatment, instituting a reliable screening strategy is paramount to facilitate early diagnosis and timely treatment, which can potentially impact patient outcomes and disease burden. More evidence is needed to underpin the validity and applicability of our proposed screening criteria in Taiwan.

## ***Haemophilus parainfluenzae* as a Potential Immunomodulatory Postbiotic for Autoimmune Diseases**

副流感嗜血桿菌做為免疫調控後生元——運用於自體免疫疾病的潛力

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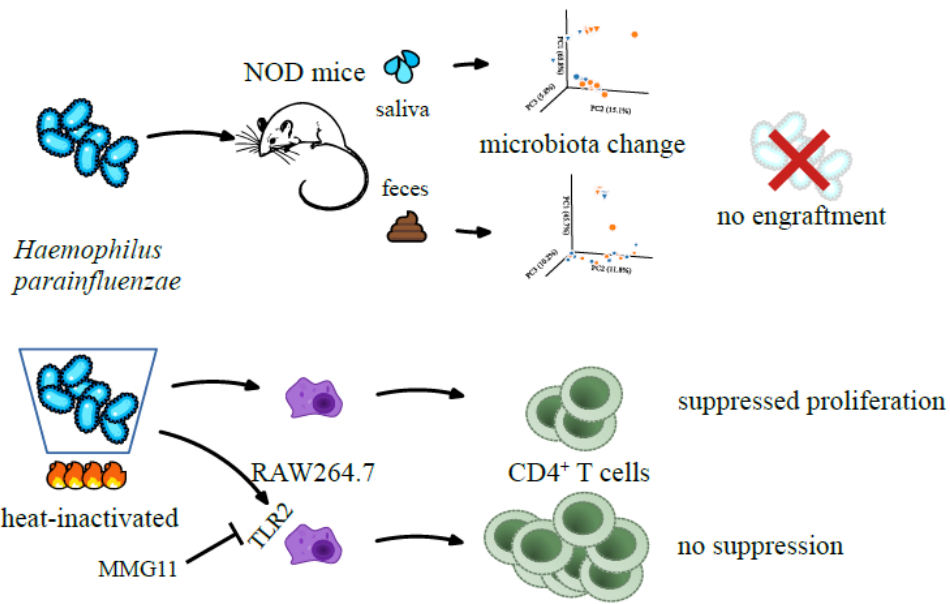
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**Background:** *Haemophilus parainfluenzae* (*Hp*) has been negatively associated with autoimmune diseases in oral microbiota studies. Previously, we demonstrated that oral *Hp* inoculation ameliorated Sjögren's syndrome-like disease in NOD mice with reduced IFN- $\gamma$ -producing T cells. A postbiotic refers to a preparation of non-living microorganisms and/or their components with a beneficial health effect. This study investigates the potential of *Hp* as a postbiotic by assessing its effects on microbiota and antigen-presenting cells.

**Methods:** Saliva and fecal samples from NOD mice two weeks after oral *Hp* inoculation were subjected to sequencing of bacterial *16S* ribosomal DNA. RAW264.7 cells were pretreated with heat-inactivated *Hp* to assess the immunomodulatory effect as a postbiotic.

**Results:** Oral *Hp* inoculation promoted species richness and diversity in the salivary microbiota, resulting in a diverged composition. Amplicons annotated to *Pseudomonas* species exhibited reduced abundances. In the fecal microbiota, species richness, evenness, and diversity remained comparable. However, the composition differed from controls, with amplicons mostly annotated to *Bacteroides* species being enriched. Intriguingly, *Hp* was nearly absent in both control and *Hp*-inoculated mice, suggesting that the protective effect did not require *Hp* engraftment. Moreover, RAW264.7 cells pretreated with heat-inactivated *Hp* suppressed CD4<sup>+</sup> T cell proliferation, and this effect was reversed by the TLR2 antagonist MMG11.

**Conclusion:** Oral *Hp* inoculation modulated the salivary and fecal microbiota in NOD mice without engraftment. Heat-inactivated *Hp* effectively regulated the CD4<sup>+</sup> T cell response through antigen-presenting cells in a TLR2-dependent manner. These findings highlight the potential of *Hp* as an immunomodulatory postbiotic for autoimmune diseases.



**Graphical Abstract** Oral inoculation of *Haemophilus parainfluenzae* in NOD mice resulted in salivary and fecal microbiota change without engraftment. Heat-inactivated *H. parainfluenzae* suppressed CD4<sup>+</sup> T cell proliferation through RAW264.7 in a TLR2-dependent manner.



**The effect of up-regulated circular RNA, hsa-RNPS1, of T cells on expression of the pro-inflammatory cytokines**

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T 細胞環狀 RNA, hsa-RNPS1, 上調表達對發炎細胞激素表達的影響

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**Background:** More than 95% AS patients carry the HLA-B27 gene. However, only 1-2% of people that are HLA-B27-positive develop ankylosing spondylitis (AS), suggesting that other genetic or environmental factors may also contribute to the development of AS. In early study, we have found that the expression of circRNA, hsa-RNPS1, in T cells of AS patients is up-regulated through analysis of high throughput RNA sequencing and quantitative real-time PCR (qRT-PCR). However, the effect of hsa-RNPS1 of T cells on expression of the pro-inflammatory cytokines remained unknown.

**Methods:** Jurkat cells were transfected with circular or linear form of hsa-RNPS1 by electroporation. The expression levels of cytokines were analyzed by qRT-PCR. The JAK/Stat1 signaling pathway was analyzed by western blotting after Jurkat cells were transfected with hsa-RNPS1.

**Results:** Overexpression of circular hsa-RNPS1 in Jurkat cell up-regulated the expression of cytokines, IL-2, IL-17 and Interferon-gamma (IFN-gamma) and activated the JAK/STAT1 signaling. However, overexpression of the linear RNPS1 in Jurkat cells failed to enhance the expression of cytokines

**Conclusion:** Up-regulation of hsa-RNPS1 expression in T cell of AS enhances the expression of proinflammatory cytokines, IL-2, IL-7 and IFN-gamma and stimulates the JAK/STAT1 signaling.

桂皮成分孜然醛对自噬的影响

**Effect of *Cinnamomum verum* component cuminaldehyde on autophagy**

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**Abstract**

**Background**

Plants produce numerous bioactive components for a variety of purposes. Plant products have been the basis of treatment of human disorders since time immemorial. Many of them have been shown to possess both antitumor and immunomodulatory activities.

In our ongoing study to identify anticancer agents from natural resources, cuminaldehyde (CuA), a constituent of the bark of the plant, was discovered to have some pharmacological activities similar to those of chloroquine (a drug possesses various immunomodulatory effects and has an established role in the management of various rheumatic diseases), including up-regulates lysosomal vacuolation with increased volume of acidic compartment (VAC) in various cell lines, suggesting a possible modulating role in autophagy.

**Methods**

Effect of *Cinnamomum verum* component cuminaldehyde on autophagy was evaluated using human lung squamous cell carcinoma NCI-H520 cells. Detections of MAP1-LC3 were performed by both Western immunoblotting and immunofluorescence.

**Results and conclusion**

Cuminaldehyde does possess autophagic activity in human lung squamous cell carcinoma NCI-H520 cells. Future direction would be exploring the potential clinical applications in various autoimmune and other diseases.

全基因組關聯研究的多層次分析顯示了自體免疫疾病的致病過程牽涉不同免疫細胞

## Multilevel Analyses of Genome-Wide Association Studies Highlight the Involvement of Different Immune Cells in Autoimmune Diseases

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曾家駿, 顏昌毅, 王品逸, 陳冠宇, 吳正欽, 歐燦騰, 蔡文展, 顏正賢, 陳忠仁, 劉宏文.

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### Abstract

**Background:** Different autoimmune diseases (ADs) have overlapped but divergent clinical manifestations. We aim to investigate the genetic overlap between ADs and if involved types of cell subsets contribute to heterogeneity between ADs.

**Methods:** We utilized tissue-specific functional enrichment to distinguish cell types that contributed to the ADs. We assessed the subset-specific genetic correlation of ADs and performed colocalization, gene identification, transcription factor (TF) annotation, pathway discovery, and network analysis to evaluate genetic overlap between ADs at the levels of variants, genes, TFs, and pathways.

**Results:** Functional enrichment singled out immune cells as the most critical players in ADs. Cell lineage-specific genetic correlation differed with leukocyte genetic correlation, led to ADs clustering distinct from obtained by leukocyte genetic correlation, and had superior ability to predict symptom differences between ADs compared with leukocyte genetic correlation. At the levels of variants, genes, TFs, and pathways, we repeatedly detected existence of genetic overlap and evidence that cellular contexts modulated genetic effects on ADs. We also discovered several drugs which exerted cell type-specific effects which contributed to drug-induced AD flares.

**Conclusion:** Actions of pathogenic factors in different immune subsets drove diverse clinical spectrum and treatment response of ADs. This indicated that besides pathogenic factors, cellular contexts were also important effectors and determinants of ADs.

**Castleman Disease: A Clinicopathologic Study of 31 Cases**

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**Background:** Castleman disease (CD) is a rare lymphocytic disorder with two subtypes: Unicentric CD (UCD) and multicentric CD (MCD). UCD has a favorable prognosis following surgical excision, while MCD presents a severe clinical course with unfavorable outcomes.

**Methods:** We retrospectively analyzed clinical data from 31 CD cases diagnosed at our institution between 2002 and 2022. Demographics, clinical variables, anatomical site, centricity, histopathology, and treatment approaches were assessed.

**Results:** Among the 31 cases, there were 19 females and 12 males, with a mean age of 51±16 years. UCD accounted for 18 cases, while MCD accounted for 13 cases, all confirmed by biopsy. Histopathological analysis revealed a hyaline vascular variant in 7 cases (25%) and a plasma cell variant in 21 cases (75%). Predominant lesion locations included the head and neck region (52%, n=16), axilla (26%, n=8), mediastinum (29%, n=9), intra-abdomen (19%, n=6), and pelvic/inguinal region (19%, n=6). Laboratory analysis demonstrated significant differences in hemoglobin, CRP, and IgG levels between UCD and MCD patients. UCD cases underwent surgical resection as the primary treatment approach (94%). Among MCD patients, 84.6% (n=11) presented with concurrent systemic symptoms, such as renal involvement (54%, n=7), splenomegaly (30%, n=4), systemic lupus erythematosus (15%, n=2), POEMS syndrome (15%, n=2), and TAFRO syndrome (n=1).

**Conclusion:** Accurate differentiation between UCD and MCD is crucial due to distinct treatment approaches. Although the study's limited number of cases is a limitation, the results, particularly the laboratory data, provide valuable insights for the initial assessment and management of CD patients.

## 海報摘要 TCR67

化膿性汗腺炎患者的長期乾癬風險：一份跨醫學中心的回溯性研究

**Long term psoriasis risk in people with hidradenitis suppurativa: a multicenter retrospective study**  
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中山醫學大學 醫學研究所

### Abstract

#### Background

The association between HS and psoriasis was not yet well developed and real-world evidences based on large-scale population-based study was lacking. This study aims to evaluate the long-term risk of psoriasis in patients with HS in the United States.

#### Methods

Electronic medical records of participants were retrieved from the TriNetX US Collaborative Network. After identifying eligible people with HS, a 1:1 propensity score matching was performed to identify HS-free control group. Within the 10-year study period, the adjusted hazard ratio (aHR) of psoriasis were calculated

#### Results

The risk of psoriasis in the HS group was 2.23 times higher than in the non-HS group within 10 years of follow-up (95% CI, 1.94-2.57). The significance of the observed association remained within a shorter follow-up time. In young adults and older patients older than 65 years, the risk of psoriasis was 2.56 (95% CI, 2.20-2.96) and 2.34 (95% CI, 1.10-4.98), respectively.

## Conclusions

The long-term risk of future psoriasis was observed in patients with HS. While caring for people with HS, clinicians were recommended to be aware of the risk of future psoriasis.

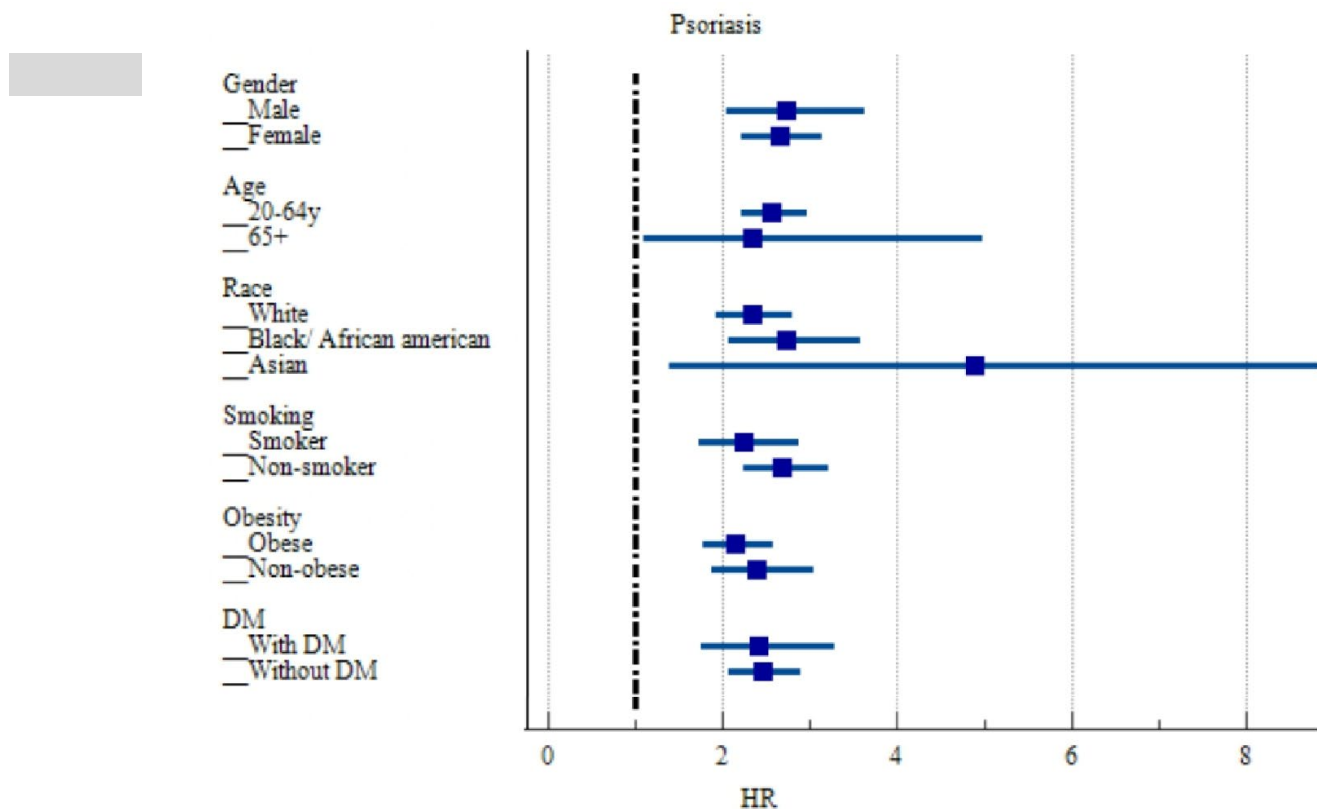
**Table 1.** Risk of psoriasis among hidradenitis suppurativa (HS) cohort compared to control cohort

| Outcome   | Cases occurring new-onset psoriasis* |                              | Adjusted hazard ratio (95% Confidence interval)** |                               |                               |
|-----------|--------------------------------------|------------------------------|---|-------------------------------|-------------------------------|
|           | HS cohort<br>(n=69,153)              | Control cohort<br>(n=69,153) | 1 year  | 5 years                       | 10 years                      |
| Psoriasis | 583                                  | 294                          | <b>2.236</b><br>(1.724-2.901)                     | <b>2.108</b><br>(1.815-2.449) | <b>2.233</b><br>(1.941-2.569) |

\*Data present here were the value of follow up from 90 days after index date to 10 years.

\*\*Propensity score matching was performed on age at index, gender, race, and social economic status (problems related to housing and economic circumstances, persons with potential health hazards related to socioeconomic and psychosocial circumstances)

**Figure 1.** Forest plot of stratification analysis of psoriasis risk in HS patients



**Risk of end-stage renal disease (ESRD) in ANCA-associated vasculitis glomerulonephritis (AAV-GN) patients**Wang, Pin-Hsuan<sup>1</sup>,

王品軒

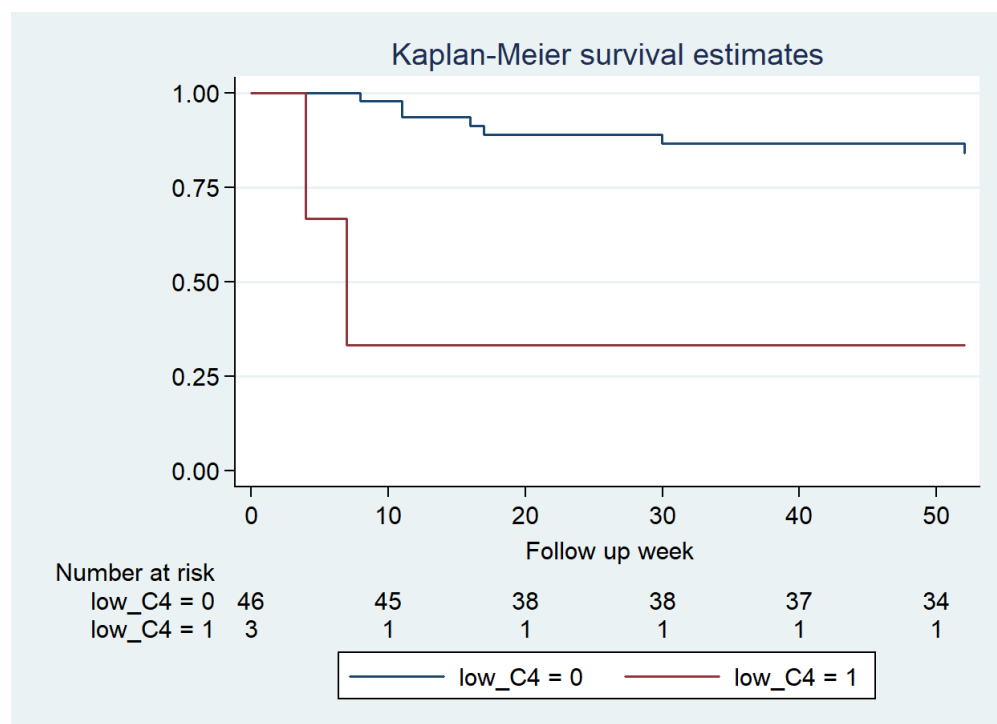
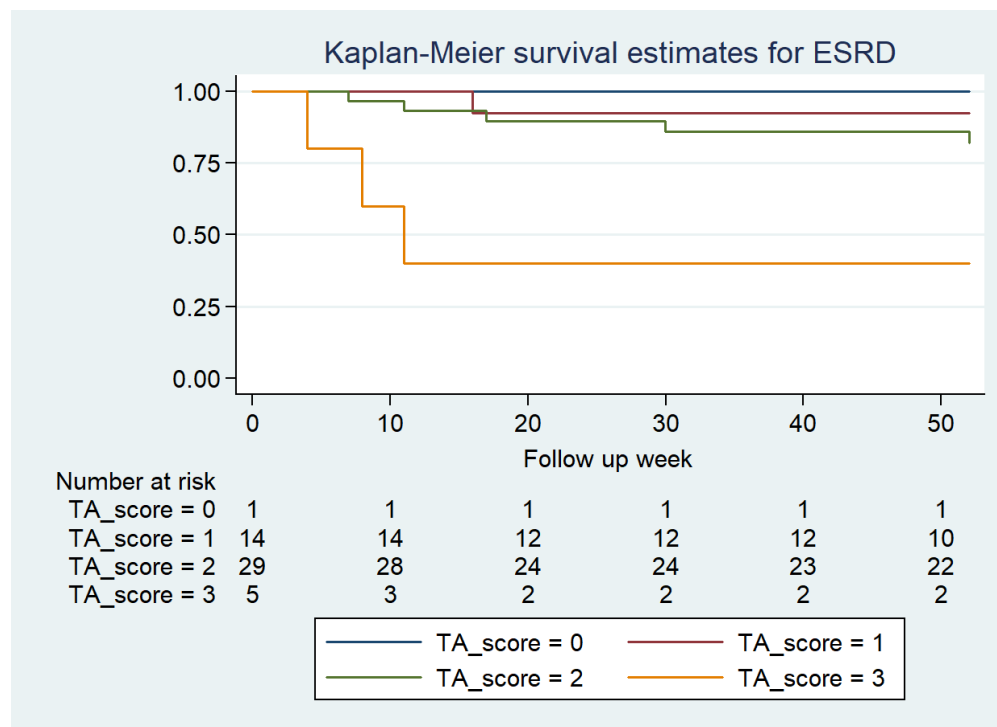
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**Abstract****Objective:** To determine the risk of end-stage renal disease (ESRD) in patients diagnosed with ANCA-associated vasculitis glomerulonephritis (AAV-GN) over a follow-up period of 52 weeks.**Methods:** In this retrospective study, we recruited patients with biopsy-proven AAV-GN between 2010 and 2022. We documented baseline clinical characteristics and laboratory data, then analyzed risk factors contributing to ESRD.**Results:** A total of 53 patients with AAV-GN (male ratio 54.7%, mean age 53 years old) were enrolled. The mean creatinine level was 3.7mg/dL. A significant majority, 52 (98.1%), tested positive for ANCA autoantibodies, including 45 (84.9%) P-ANCA and 7 (13.2%) C-ANCA. Of all patients, 32 (60.4%) underwent cyclophosphamide treatment, 26 (49.1%) rituximab, and 21 (39.6%) plasmapheresis. During the mean follow-up period of 40 weeks, 13 (24.5%) patients progressed to ESRD. All patients presented with at least one pathohistological manifestation of tubulointerstitial change. According to multivariate Cox regression analysis, the risk factors for ESRD included elevated serum creatinine levels (Hazard ratio [HR] 1.3, 95% confidence interval [CI] 1.06-1.60,  $p=0.012$ ), complement C4 below 10mg/dL (HR 5.6, 95% CI 1.05-29.97,  $p=0.043$ ), and elevated tubular atrophy scores (HR 3.3, 95% CI 1.20-8.98,  $p=0.020$ ).**Conclusion:** A high incidence rate of ESRD was observed in patients with AAV-GN. Risk factors identified include increased serum creatinine levels, low complement C4, and high tubular atrophy scores. Aggressive treatment should be considered in the high-risk patients.**Table 1** Risk factors analyses for poor renal outcome in ANCA-associated glomerulonephritis patients.

| Parameter                      | Univariate analysis |            |                 | Multivariate analysis |            |                 |
|--------------------------------|---------------------|------------|-----------------|-----------------------|------------|-----------------|
|                                | HR                  | 95% CI     | <i>p</i> -value | HR                    | 95% CI     | <i>p</i> -value |
| Age > 60 years                 | 2.5                 | 0.76-7.96  | 0.136           |                       |            |                 |
| Creatinine, mg/dL              | 1.2                 | 1.05-1.49  | 0.012           | 1.3                   | 1.06-1.60  | 0.012           |
| Albumin < 3.5g/dL              | 2.1                 | 0.58-7.69  | 0.257           |                       |            |                 |
| Neutrophil-to-lymphocyte ratio | 1.3                 | 1.44-4.08  | 0.615           |                       |            |                 |
| Complement C3 < 90mg/dL        | 1.9                 | 0.61-5.73  | 0.271           |                       |            |                 |
| Complement C4 < 10mg/dL        | 4.7                 | 1.02-21.55 | 0.047           | 5.6                   | 1.05-29.97 | 0.043           |
| Interstitial fibrosis score    | 2.0                 | 0.78-5.33  | 0.147           |                       |            |                 |
| Inflammatory change score      | 1.4                 | 0.68-3.00  | 0.353           |                       |            |                 |
| Tubular atrophy score          | 3.7                 | 1.45-9.46  | 0.006           | 3.3                   | 1.20-8.98  | 0.020           |

**Figure 1** Kaplan–Meier survival estimates of ANCA-associated glomerulonephritis patients according to tubular atrophy score and low complement C4





## Association of Dipeptidyl Peptidase-4 Inhibitor Use for Type 2 Diabetes Mellitus and Incidence of Osteoarthritis in Taiwan

台灣第二型糖尿病患者使用二肽基肽酶-4 抑制劑與退化性骨關節炎發生率的關聯性研究

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### Background

Cellular senescence is involved in osteoarthritis (OA) development. Dipeptidyl Peptidase-4 (DPP4) is associated with chondrocyte senescence. It is uncertain whether DPP4 inhibitor (DPP4i) use is associated with reduced risk of OA in patients with type 2 diabetes mellitus (T2DM). We aimed to establish whether DPP4i use was associated with a reduced risk of OA among these patients.

### Methods

We selected T2DM patients diagnosed between 2008-2018 from the Taiwan National Health Insurance Research Database. We used individual matching (1:1), age  $\pm 1$ , same gender, same index year, and same diabetes complications severity index to balance potential confounders between DPP4i users and nonusers. We assessed the risks of OA using Cox proportional hazards regression between DPP4i users and nonusers.

### Results

We included 166,987 participants not treated with DPP4i and 166,987 treated with DPP4i (mean age 58.60 yr, standard deviation 9.53 yr). In the DPP4i user cohort, 5953 patients developed OA during a median follow-up of 3.61 years and had lower risks of incident OA (adjusted hazard ratio [HR] 0.43, 95% confidence interval [CI] 0.42-0.45). Furthermore, the use of concurrent medications, such as glucagon-like peptide-1 receptor agonist (0.22 [0.15-0.31]) and corticosteroid (0.66 [0.64-0.68]), was associated with a lower OA risk. We observed no dose-dependent effect of DPP4i use and OA.

### Conclusions

DPP4i use in patients with T2DM was associated with a significantly reduced risk of OA. Randomized controlled trials in patients with OA are warranted to determine whether DPP4i effectively decreases the incidence of OA.

## A Case of VEXAS Syndrome caused by a UBA1 Somatic Mutation

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### Background:

VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome was first described in 2020 as late onset, acquired autoinflammatory disorder caused by mutations in the UBA1 gene. The various clinical manifestations of VEXAS broadly divided into inflammatory or hematological which can cause multi-organ involvement.

### Case Presentation:

A 75-years-old male patient presented with first symptoms of dermatitis and joint pain in September 2020. In 2021 July, he started to develop intermittent fever along with persisted joint pain, erythematous skin rash, anemia, mild leukopenia, raised inflammatory markers (CRP 8.33 mg/dL; ESR 114 mm/hr; Hb 8.7 g/dl). Skin biopsy revealed neutrophilic dermatosis and leukocytoclastic vasculitis. Bone marrow examination showed mild hypercellular marrow with myeloid vacuolization without evidence of a plasma cell dyscrasia (figure 1). His symptoms were relieved with prednisolone 15-20 mg/day. The patient remained transfusion dependent. His dermatitis, polyarthritis, anemia flared upon steroid tapering to below 15 mg/day with markedly elevated inflammation markers. He was subsequently initiated on hydroxychloroquine (HCQ) and methotrexate (MTX) for steroid sparing. In 2023, he was diagnosed with VEXAS syndrome based on missense mutation of UBA1 gene (figure 2). The patient's VEXAS symptoms were controlled with low dose prednisolone, MTX 15mg/day and HCQ 400mg/day.

### Conclusion:

This is the first Taiwanese case of VEXAS syndrome. Rheumatologist should always consider VEXAS syndrome in male patients with late-onset inflammatory symptoms, skin involvement and hematologic abnormalities (macrocytic anemia) who respond to steroids.

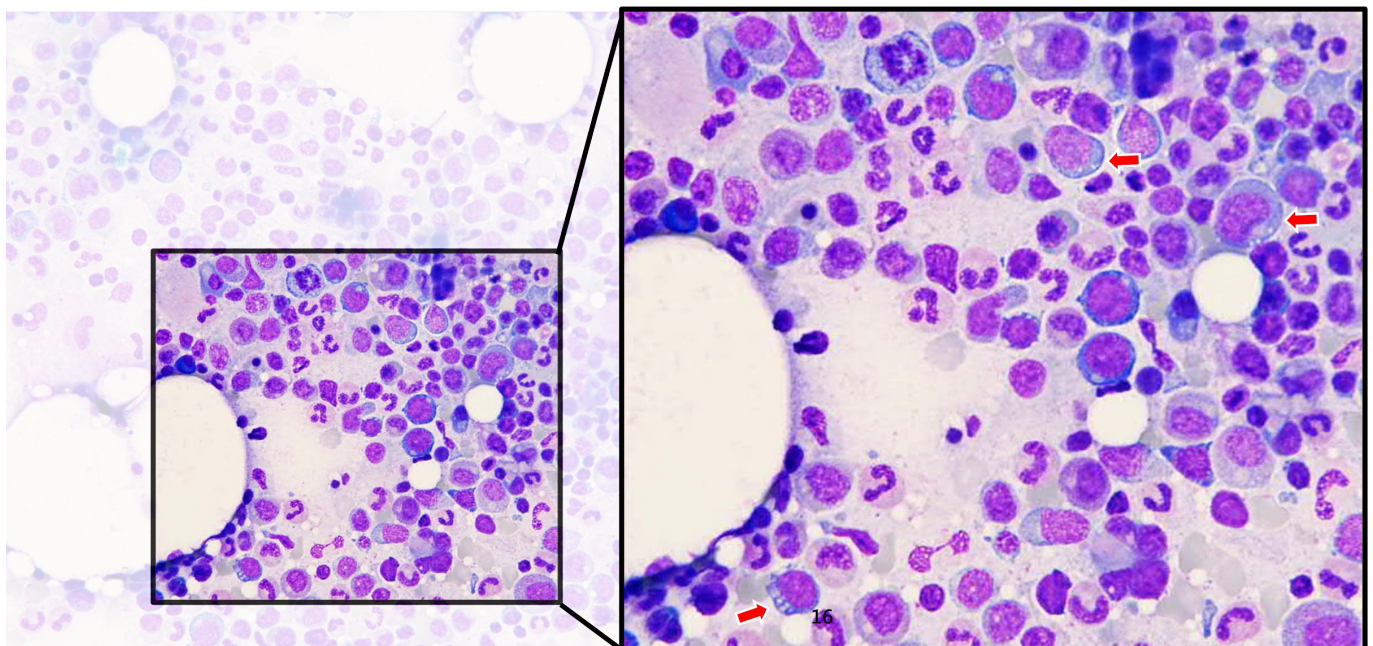


Figure 1. Bone Marrow biopsy showed myeloid vacuolization (red arrow)

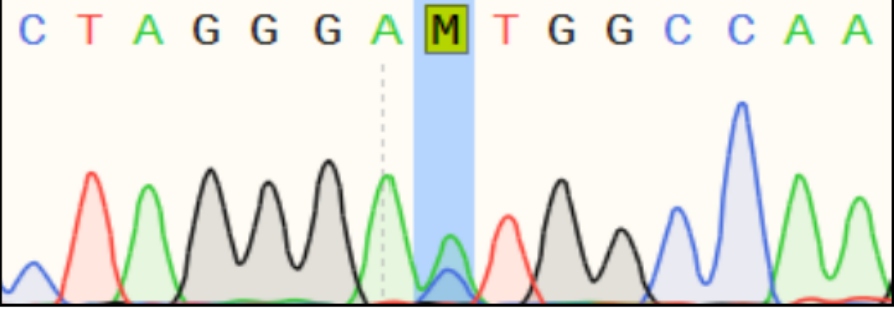
| 變異區域圖譜   | 基因型   |
|--|---|
|  | <p data-bbox="1145 488 1455 609">c.121A&gt;C<br/>(p.MET41Leu)</p> |

Figure 2. Sanger sequencing analysis showed codon 41, UBA1 gene missense mutation

## Combination of High-dose Steroid and IVIG in COVID-19-Associated Autoimmune Encephalitis: A Case Report and Literature Review

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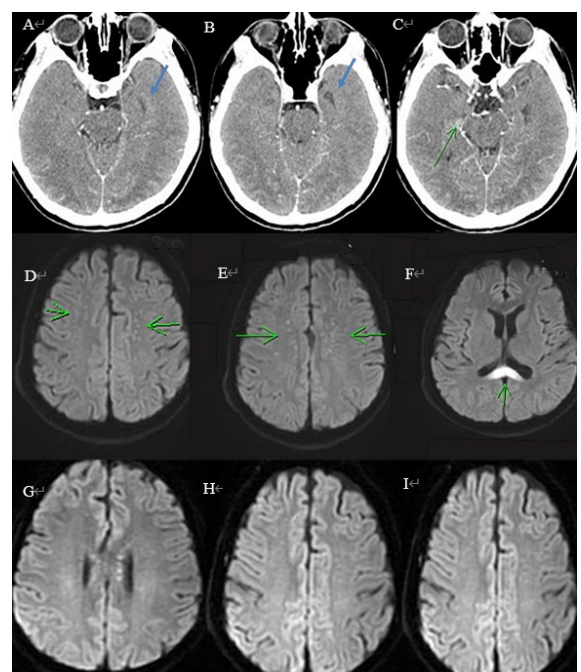
**Background:** COVID-19 has been found to induce autoimmune disorders in different organs, including autoimmune encephalitis. These immune-mediated disorders, despite not being directly related to the severity of the infection (such as respiratory symptoms), are associated with high mortality rates and poor prognoses.

**Report of Case:** A 22-year-old Taiwanese male with history of COVID-19 was transferred to ICU due to neurological symptoms including decreased consciousness (E1V1M1) and quadriplegia. Brain CT and MRI indicate inflammation in the brain, while examinations for common infectious pathogens and autoantibodies associated with autoimmune encephalitis yielded negative results. Based on the Graus criteria, he was diagnosed with encephalitis. Combination therapy of high dose steroid and IVIG was initiated, and the level of consciousness improved to E4VeM6 within three days. The strength of the upper limb muscles gradually improved from 1/5 to 2/5. Brain MRI also showed a mild regression of encephalitis. The patient was discharged with neurological sequelae, including decreased lower limb power (2/5) with urinary retention and completely recovered after rehabilitation.

**Conclusion:** Limited clinical evidence exists regarding the effectiveness and safety of combining IVIG and corticosteroids in treating COVID-19-related autoimmune encephalitis. The case had a positive outcome after administered the combined therapy. Although data and guidelines are lacking, using high-dose steroids and IVIG as a therapeutic approach could be beneficial for patients with COVID-19-associated autoimmune encephalitis.

### Figure 1

Brain CT (image A-C) Brain MRI (image D-F) showing sign of encephalitis. Image G-I showing regression of inflammation after administrating high dose steroid and IVIG.



**Factors associated with subclinical inflammation of wrist joints in rheumatoid arthritis patients with low or no disease activity- A RA ultrasound registry study**

影響低疾病活性類風濕關節炎超音波出現潛藏發炎的因子

陳英州 鄭添財 賴漢明 尤珊富 許鐘元 柯祈化 陳嘉峯 邱文燦 王鈺維

Ying-Chou Chen , Tien-Tsai Cheng, Han-Ming Lai, Shan-Fu Yu, Wen-Chan Chiu, Chung-Yuan Hsu, Jia-Feng Chen, YW, Wang

高雄長庚風濕免疫科

**Background:** To evaluate the factors to predict subclinical inflammation of wrist joints in patients with RA who are in clinical remission or low disease activity

**Methods:** Gray scale and power Doppler ultrasound were performed on the dorsal radio-lunate of both wrists. The presence of synovitis, comorbidities, and use of disease modifying anti-rheumatic drugs were recorded. A Multivariable forward logistical regression model was used to identify factors associated with subclinical inflammation.

**Results:** There were 1248 patients (1010 females, 238 males; mean age:  $60.0 \pm 10.5$  years ). 57.4% of patients in complete remission and low disease activity had sonographic inflammation. Multivariable forward logistic regression analysis indicated that male sex, smoking are positively associated with inflammation and that age, alcohol consumption, and use of methotrexate, glucocorticoid, or a biological therapy are negatively associated with inflammation. Use of biological agents decreased the risk of inflammation by 40.9%.

**Conclusions:** There was evidence of subclinical inflammation in most patients who were in low or no disease activity, those with biological therapy had lower risk of subclinical inflammation.

**Keywords:** subclinical inflammation, rheumatoid arthritis, ultrasound, DAS 28, disease activity

**Table .** Multivariable forward logistic regression analysis of factors associated with subclinical inflammation.

| Variable                             | Regression coefficient | Standard error | Wald  | p value | Odd ratio (95% CI) |
|--------------------------------------|------------------------|----------------|-------|---------|--------------------|
| Sex                                  | 0.52                   | 0.10           | 23.93 | 0.001   | 1.69(1.37-2.09)    |
| Age                                  | -0.01                  | 0.00           | 13.48 | 0.001   | 0.98 (0.98-0.99)   |
| Body mass index (kg/m <sup>2</sup> ) | -0.01                  | 0.00           | 0.56  | 0.451   | 0.99 (0.97-1.01)   |
| Smoking                              | 0.52                   | 0.16           | 9.69  | 0.002   | 1.69 (1.21-2.35)   |
| Alcohol consumption                  | -0.59                  | 0.21           | 7.44  | 0.006   | 0.55(0.35-0.84)    |
| Methotrexate                         | -0.18                  | 0.07           | 5.45  | 0.020   | 0.83(0.71-0.97)    |
| Hydroxychloroquine                   | 0.07                   | 0.07           | 0.94  | 0.332   | 1.07 (0.93-1.23)   |
| Sulphasalazine                       | -0.28                  | 0.16           | 2.86  | 0.091   | 0.75 (0.54-1.04)   |
| Leflunomide                          | 0.05                   | 0.10           | 0.24  | 0.622   | 1.05 (0.42-1.100)  |
| Cyclosporine                         | -0.64                  | 0.46           | 1.88  | 0.170   | 0.52 (0.21-1.31)   |
| Glucocorticoid use                   | -0.50                  | 0.07           | 48.27 | 0.001   | 0.60(0.52-0.69)    |
| Biological therapy                   | -0.52                  | 0.07           | 48.83 | 0.001   | 0.59 (0.50-0.68)   |

**Association of anti-ssa antibody with knee hyperemia in rheumatic clinic by propensity score matching- A registry study of *musculoskeletal* ultrasound**

傾向分析 Anti-ssa 抗體和超音波膝關節血流增加有相關：一份風濕關節超音波的登記研究結果

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**Background:**

Autoimmune disease, characterized by autoantibodies including Sjogren's syndrome (SS)-related antigen A (SSA, also called Ro), affects multiple organs systems. Abnormally increased blood flow in musculoskeletal disease indicates a potential association between blood flow velocity and pain. This study evaluated the association between SSA positivity and joint hyperemia in rheumatic clinic.

**Research design and methods**

This is a registry study. We collected patients at rheumatic who underwent complete assessment according to standard protocol. Clinical history included autoimmune disease-related features and comorbidities. SSA and anti-nuclear antigen (ANA) were tested. Ultrasound (US) was employed to observe structural changes in the knee joints and tendons along the longitudinal and transverse planes. Power Doppler (PD) measured blood flow, with  $PD \geq 1$  indicating hyperemia.

**Results:**

In total, 1256 patients were enrolled, including 200 with rheumatoid arthritis (RA) and 512 with SS. Propensity score matching, based on age, sex, body mass index (BMI), and RA, identified 60 SSA-positive and 60 matched SSA-negative patients. The SSA-positive group had higher ANA ( $p < 0.001$ ) and hyperemia in both left and right knees on both lateral and medial sides compared with the SSA-negative group ( $p < 0.001$ ). On logistic regression, ANA was associated with increased SSA [ $p = 0.001$ ; OR, 14.84 (3.06–72.01)], and left lateral [ $p = 0.001$ ; OR, 69.62 (7.86–617.06)] and medial knee hyperemia [ $p = 0.001$ ; OR, 17.02 (3.35–86.42)] increased SSA risk.

**Conclusion**

Knee hyperemia is highly correlated with SSA, with characteristic musculoskeletal US outcomes. This study will contribute to the increased application of musculoskeletal US to detect hyperemia in SSA-positive patients.

**Key words:** Anti-SSA, hyperemia, knee, ultrasound, propensity score

**Table 1. Characteristics of the study patients**

| Variables                                       | SSA (n = 60)  | No SSA (n = 60) | P-value |
|---|---------------|-----------------|---------|
| Age (years), mean ± SD                          | 59.93 ± 10.32 | 58.8 ± 8.02     | 0.503   |
| Body mass index (kg/m <sup>2</sup> ), mean ± SD | 23.09 ± 3.23  | 23.77 ± 3.29    | 0.26    |
| Sex (Female %)                                  | 56 (93.3)     | 56 (93.3)       | 1       |
| Anti-nuclear antibody (n, %)                    | 28 (46.7)     | 16 (26.7)       | 0.003   |
| Diabetes mellitus (n, %)                        | 8 (13.3)      | 12 (20.0)       | 0.232   |
| Hypertension (n, %)                             | 8 (13.3)      | 4 (6.7)         | 0.181   |
| Rheumatoid arthritis (n, %)                     | 48 (80)       | 48 (80)         | 1       |
| Hyperemia over left medial knee (n, %)          | 52 (86.7)     | 32 (53.3)       | <0.001  |
| Hyperemia over left lateral knee (n, %)         | 56 (93.3)     | 36 (60.0)       | <0.001  |
| Hyperemia over right medial knee (n, %)         | 56 (93.3)     | 44 (73.3)       | 0.006   |
| Hyperemia over right lateral knee (n, %)        | 44 (73.3)     | 28 (46.7)       | 0.005   |

Abbreviations: SSA, Sjogren syndrome-related antigen A; SD, standard deviation

**Table 2. Factors influencing SSA**

| Variables         | Regression coefficient | SE   | Wald  | P-value | OR (95 CI)          |
|-------------------|------------------------|------|-------|---------|---------------------|
| Age               | 0.05                   | 0.04 | 1.34  | 0.247   | 1.05 (0.97–1.15)    |
| Body mass index   | -0.02                  | 0.15 | 0.02  | 0.899   | 0.98 (0.73–1.32)    |
| ANA               | 2.70                   | 0.81 | 11.21 | 0.001   | 14.84 (3.06–72.01)  |
| Diabetes mellitus | -0.13                  | 0.86 | 0.02  | 0.876   | 0.87 (0.16–4.7)     |
| Hypertension      | 0.67                   | 1.07 | 0.39  | 0.534   | 1.95 (0.24–15.96)   |
| LL                | 4.24                   | 1.11 | 14.53 | <0.001  | 69.62 (7.86–617.06) |
| LM                | 2.83                   | 0.83 | 11.69 | 0.001   | 17.02 (3.35–86.42)  |
| RL                | -0.71                  | 0.95 | 0.56  | 0.454   | 0.49 (0.08–3.17)    |
| RM                | 0.22                   | 0.87 | 0.07  | 0.798   | 1.25 (0.23–6.81)    |

Abbreviations: OR, Odds ratio; SE, standard error; SSA, Sjogren's syndrome-related antigen A; 95 CI, 95% Confidence interval; ANA, anti-nuclear antigen; LL, left lateral knee; LM, left medial knee; RL, right lateral knee; RM, right medial knee