Temporomandibular Internal Derangements Denote Activity of Axial Spondyloarthritis

Laškarin, Ana-Marija; Špalj, Stjepan; Laškarin, Gordana; Ružić Baršić, Antonija; Grđan, Jasmina; Babarović, Emina; Kehler, Tatjana; Peršić, Viktor; Dulčić, Nikša

Source / Izvornik: **Acta stomatologica Croatica : International journal of oral sciences and dental medicine, 2025, 59, 2 - 14**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.15644/asc59/1/1

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:184:337784

ACTA
STOMATOLOGICA
CROATICA
www.ascro.hr

Acta stomatol Croat. 2025;59(1):2-14.
DOI: 10.15644/asc59/1/1

ORIGINAL SCIENTIFIC PAPER
IZVORNI ZNANSTVENI RAD

Ana-Marija Laškarin[1], Stjepan Špalj[2,3], Gordana Laskarin[4,5], Antonija Ružić Baršić[5], Jasmina Grđan[5], Emina Babarović[6], Tatjana Kehler[5,7], Viktor Peršić[5,7], Nikša Dulčić[8]

Temporomandibular Internal Derangements Denote Activity of Axial Spondyloarthritis

Intrakapsularni temporomandibularni poremećaji označavaju aktivnost aksijalnog spondiloartritisa

[1] PhD student, School of Dental Medicine University of Zagreb, Zagreb, Croatia
Doktorandica Stomatološkog fakulteta Sveučilišta u Zagrebu, Zagreb, Hrvatska
[2] Department of Orthodontics, Faculty of Dental Medicine, University of Rijeka, Rijeka, Croatia
Katedra za ortodonciju Fakulteta dentalne medicine Sveučilišta u Rijeci, Rijeka, Hrvatska
[3] Department of Dental Medicine, Faculty of Dental Medicine and Health, J. J. Strossmayer University of Osijek, Osijek, Croatia
Katedra za dentalnu medicinu Fakulteta dentalne medicine i zdravstva Sveučilišta J. J. Strossmayer u Osijeku, Osijek, Hrvatska
[4] Department of Physiology, Immunology and Pathophysiology, Faculty of Medicine, University of Rijeka, Rijeka, Croatia
Zavod za fiziologiju, imunologiju i patofiziologiju Medicinskog fakulteta Sveučilišta u Rijeci, Rijeka, Hrvatska
[5] Hospital for Medical Rehabilitation of Heart and Lung Diseases and Rheumatism "Thalassotherapia-Opatija", Opatija, Croatia
Bolnica za medicinsku rehabilitaciju srčanih i plućnih bolesti i reumatizma Thalassotherapia-Opatija, Opatija, Hrvatska
[6] Department of Pathology, Clinical Hospital Center, University of Rijeka, Rijeka, Croatia
Klinika za patologiju Kliničkoga bolničkoga centra Sveučilišta u Rijeci, Rijeka, Hrvatska
[7] Department of Medical Rehabilitation, Faculty of Medicine, University of Rijeka, Rijeka, Croatia
Zavod za medicinsku rehabilitaciju Medicinskog fakulteta Sveučilišta u Rijeci, Rijeka, Hrvatska
[8] Department of Removable Prosthodontics, School of Dental Medicine University of Zagreb, Zagreb, Croatia
Zavod za mobilnu protetiku Stomatološkog fakulteta Sveučilišta u Zagrebu, Zagreb, Hrvatska

Abstract

Objectives: The group of spondyloarthritis (SpA) disorders shares common clinical manifestations, including internal derangement (ID) of temporomandibular joint (TMJ). This study aimed to investigate SpA activity in patients with ID of TMJ. **Materials and Methods:** We assessed 200 patients with neck pain using the Assessment of Spondyloarthritis International Society (ASAS) criteria. TMJ was examined using Diagnostic Criteria for Temporomandibular Disorders (DC/TMD protocol). Patients with SpA were divided into three groups: symptomatic ID of TMJ, asymptomatic ID of TMJ, or healthy TMJ (controls). Activity of SpA was evaluated using the Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Disease Activity Index in Psoriatic Arthritis (DAPSA), patients' self-estimated SpA activity, difficulties in performing daily activities, pain intensity (visual analogue scale) and laboratory parameters. **Results:** Patients with symptomatic and asymptomatic ID showed statistically significantly increased ASDAS, anti-streptolysin titer, patients' self-estimated axial pain and activity of SpA, and decreased hematocrit than the control. Patients with symptomatic ID also had statistically significant earlier onset of SpA, along with increased BASDAI and DAPSA, total body pain, difficulties in performing daily activities, platelet count, and serum alpha-amylase but lower hemoglobin concentration than controls. Patients with asymptomatic ID had higher frequencies of exacerbated axial SpA and sacroiliac joint ankylosis compared to the control. **Conclusion:** All patients with SpA and ID showed increased axial disease activity.

Received: October 17, 2024
Accepted: March 2, 2025

Address for correspondence
Ana-Marija Laškarin, DMD, PhD student
University of Zagreb
School of Dental Medicine
Gundulićeva 5, HR-10000 Zagreb
Phone: +385 91 790 5139
alaskarin@sfzg.hr

MeSH Terms: Temporomandibular Joint Disorders; Axial Spondyloarthritis
Author Keywords: Internal derangement; Spondyloarthritis; Temporomandibular disorders

Ana-Marija Laškarin ORCID 0009-0004-0856-0384
Stjepan Špalj ORCID 0000-0003-4836-3903
Gordana Laskarin ORCID 0000-0002-6134-155X
Antonija Ružić Baršić ORCID 0000-0002-3035-3363
Jasmina Grđan ORCID 0009-0004-4912-2073
Emina Babarović ORCID 0000-0002-1787-2177
Tatjana Kehler ORCID 0000-0003-4228-1632
Viktor Peršić ORCID 0000-0003-4473-5431
Nikša Dulčić ORCID 0000-0002-8536-000X

Introduction

Spondyloarthritis (SpA) encompasses a group of related immune disorders with similar etiopathogenetic mechanisms and clinical manifestations (1), including HLA-B27+ SpA, reactive arthritis, psoriatic arthritis, enteropathic SpA associated with intestinal inflammation, and undifferentiated SpA (2). A genetic predisposition, notably the expres-

Uvod

Spondiloartritis (SpA) obuhvaća skupinu srodnih imunosnih poremećaja sa sličnim etiopatogenetskim mehanizmima i kliničkim pojavnostima (1), uključujući *HLA-B27* + SpA, reaktivni artritis, psorijatični artritis, enteropatski SpA povezan s upalom crijeva i nediferencirani SpA (2). Genetska sklonost, posebice sklonost gena *HLA-B8*, *B27, B38* i *B39*

sion of HLA-B8, B27, B38, and B39 genes, explains the onset of the disease in young adults (3), as verified by magnetic resonance imaging (MRI) and classified as non-radiological axial (nr-ax) SpA (4). All the above-mentioned forms of SpA can manifest as temporomandibular disorders (TMDs), which have recently been recognized as more than localized inflammation or disorders, instead representing a pathological process underlying the axial form of SpA (5). Untreated nr-axSpA can lead to structural changes in the spine, detectable through radiography and represent radiographic axial (r-ax) SpA or ankylosing spondylitis (4). Radiographic axSpA is characterised by erosion, fat metaplasia, and ankylosis of the sacroiliac joints and/or spine (6). Not all nr-axSpA cases progress to r-axSpA, with progression likely dependent on the severity of damage (4). Pain in the spine or peripheral joints in the peripheral form of the disease is the primary symptom that prompts patients with SpA to consult a rheumatologist and is evaluated at every examination. Axial SpA usually starts as inflammatory low back pain and gradually spreads up the spine (4). Thus, patients with axial SpA often report varying intensities of neck pain radiating to the shoulders and head, including orofacial pain (7). They may also report difficulties with neck movements associated with difficulties in opening or closing the mouth, pain, stiffness, clicking and/or crepitus in the temporomandibular joints (TMJs), and sensitivity of the masticatory muscles (8).

Currently, the relationship between TMDs and SpA is not entirely understood. The most frequent TMDs can be grouped as (I) disorders related to muscle and joint pain and headaches, and (II) intracapsular disorders related to changes in the position of the intra-articular disc and degenerative changes (9). The intracapsular disorder is also called internal derangement (ID) of the temporomandibular joint (TMJ), and cause chronic pain, clicking or crepitations, respectively (9, 10, 11). The disorders related to muscle and joint pain and headaches can coexist with ID (9, 12). The ID of TMJ has a multifactorial origin, involving a combination of biological and mechanical factors (12, 13, 14), psychological and social factors (15, 16), and synovitis (17). These factors contribute variably to the pathogenesis of TMDs, collectively causing orofacial pain, masticatory dysfunction, and communication disorders (11, 15). Despite the potential for symptomatic reactive infectious arthritis of the TMJs (18), ID was previously regarded primarily as non-inflammatory disc dysfunction, even in symptomatic subjects (19). Recently, sterile synovitis emerged as one of the significant causes of pain in axial SpA (20, 21, 22), including the pain in the TMJ (23, 24, 25). Whether the ID of TMJ represents SpA activity remains unknown. Therefore, patients with SpA exhibiting clinically pronounced disturbances of the cervical spine represent a suitable group for the study of symptomatic and asymptomatic IDs. In this investigation, we analysed the activity of SpA in symptomatic and asymptomatic IDs and compared these findings with those from patients with healthy TMJs.

za nastanak SpA-a, objašnjava početak bolesti kad je riječ o mladim odraslim osobama (3), što je potvrđeno magnetskom rezonancijom (MR) i razvrstano kao neradiološki aksijalni (nr-ax) spondiloartritis SpA (4). Svi spomenuti oblici te bolesti mogu se pojaviti u obliku temporomandibularnog poremećaja (TMP), koji se u posljednje vrijeme shvaća kao dio patološkog procesa aksijalnoga oblika SpA-a, a ne samo kao lokalizirana upala ili poremećaj (5). Ako se nr-axSpA ne liječi, može rezultirati strukturnim promjenama u kralježnici vidljivima radiografijom i predstavljati radiografski aksijalni (r-ax) spondiloartritis ili ankilozantni spondilitis (4). Za radiografsku axSpA svojstvene su erozije, masna metaplazija i ankiloza sakroilijačnih zglobova i/ili kralježnice (6). Svi slučajevi nr-axSpA-e ne napreduju u r-axSpA, pri čemu napredovanje vjerojatno ovisi o težini oštećenja (4).

Bolovi u kralježnici ili perifernim zglobovima u perifernom obliku bolesti primarni su simptom koji bolesnika sa SpA-om dovodi na pregled reumatologu i procjenjuju se tijekom svakog pregleda. Aksijalni oblik SpA obično počinje kao upalna bol u donjem dijelu leđa i postupno se širi uz kralježnicu (4). Zato bolesnici s tim oblikom SpA-a često prijavljuju bolove različite jakosti u vratu koji se šire u ramena i glavu, uključujući lice i usta (7). Također se mogu pojaviti poteškoće s pokretima vrata povezane s problemima pri otvaranju ili zatvaranju usta, bol, ukočenost, škljocanje i/ili pucketanje u temporomandibularnim zglobovima (TMZ) i osjetljivost mišića žvakača (8). Trenutačno odnos između TMP-a i SpA-e nije potpuno shvaćen. Najčešći TMP-ovi mogu se grupirati kao (I) poremećaji povezani s bolovima u mišićima i zglobovima te glavoboljom i (II) unutarzglobni poremećaji povezani s promjenama položaja unutarzglobne pločice i degenerativnim promjenama (9). Unutarzglobni poremećaj TMZ-a naziva se i intrakapsularni temporomandibularni poremećaj (IK TMP), a uzrokuje kroničnu bol, škljocanje ili pucketanje (9, 10, 11). Poremećaji povezani s bolovima u mišićima i zglobovima te glavoboljom u temporalnoj regiji mogu se pojaviti istodobno s IK TMP-om (9, 12). Više čimbenika može prouzročiti IK TMP, uključujući kombinaciju bioloških i mehaničkih čimbenika (12, 13, 14), psiholoških i društvenih čimbenika (15, 16) i sinovitisa (17). Ti čimbenici različito pridonose patogenezi TMP-a, a zajedno uzrokuju bolove usta i lica te poremećaje u žvakanju i komunikaciji (11, 15). Unatoč mogućnosti za simptomatski reaktivni infektivni artritis TMZ-a (18), IK TMP prije se smatrao primarno neupalnim poremećajem djelovanja pločice, čak i kod simptomatskih bolesnika (19). Odnedavno se sterilni sinovitis prepoznaje kao jedan od značajnih uzroka boli u aksijalnom SpA-u (20, 21, 22), uključujući i TMZ (23, 24, 25). Ostaje nepoznato je li IK TMP posljedica aktivnosti SpA-a. Zato su bolesnici sa SpA-om koji pokazuju klinički izražene poremećaje vratne kralježnice pogodna skupina za proučavanje simptomatskih i asimptomatskih IK TMP-ova. U ovom smo istraživanju analizirali aktivnost SpA-a u simptomatskim i asimptomatskim IK TMP i usporedili te nalaze s onima bolesnika sa zdravim TMZ-ima.

Material and Methods

Patients

The Ethics Committee of the Special Hospital "Thalassotherapia-Opatija," Opatija, Croatia, approved this research (approval number 01-000-00-17/2-2021) on February 10, 2021. Patients with axial and/or peripheral SpA were recruited from the Rheumatology Department of the Special Hospital for Medical Rehabilitation of Heart, Lung, and Rheumatism, "Thalassotherapia-Opatija," Opatija, Croatia, between February 10, 2021 and February 28, 2023, after a clinical rheumatological examination and an examination of their laboratory findings. The inclusion criteria were pain in the cervical spine and age between 18 and 80 years. The exclusion criteria were: rheumatoid arthritis**,** systemic connective tissue diseases, immunodeficiency, acute infection, pregnancy, malignancy within the last 5 years, uncontrolled diabetes (plasma glucose > 11 mmol/L), uncontrolled arterial hypertension (> 160/100 mmHg), acute coronary events**,** grade III and IV heart failure according to the New York Heart Association, grade IV and V renal failure, liver lesions (ALT, AST, and GGT three or more times the upper limit of normal), to avoid a significant change in the immune system other than SpA. Patients with congenital/developmental disorders of the TMJs were also excluded. Based on these criteria, 233 patients with SpA were recruited. They provided informed consent for participation, and were referred to a dental medicine specialist for clinical examination of the TMJs. This study adhered to all applicable guidelines aimed at ensuring the proper conduct and safety of participants, including the Helsinki Declaration of the World Medical Association (Edinburgh, 2000). During this study, patients did not change their regular therapy or take additional substances/drugs (placebo).

Rheumatological examination

A rheumatologist examined the patients and diagnosed SpA according to The Assessment of SpondyloArthritis International Society (ASAS) classification criteria (26). The following data were recorded: age (years), sex, body mass index (BMI, kg/m^2), duration of SpA, age at onset of SpA (years), and current therapy according to the electronic hospital information system (WinBis, IN2 Ltd., Zagreb, Croatia). Current SpA activity was assessed using the Ankylosing Spondylitis Disease Activity Score (ASDAS), patients' self-estimated axial and peripheral pain intensity, SpA activity (visual analogue scale [VAS] from 1 to 10) (27), and total body pain (visual analogue scale from 1 to 100 mm). The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used to assess neck pain (28). The Disease Activity Index for Psoriatic Arthritis (DAPSA) (29) was calculated. We also recorded the patient's difficulties in performing daily activities (VAS 1-10).

Laboratory analyses

Laboratory analyses were performed using a single 12 mL peripheral venous blood sample obtained from the cubital vein. Erythrocyte, leukocyte, and platelet cell counts, as well as hematocrit and hemoglobin concentrations, were

Materijal i metode

Bolesnici

Etičko povjerenstvo Specijalne bolnice Thalassotherapia-Opatija (Opatija, Hrvatska) odobrilo je ovo istraživanje (broj odobrenja 01-000-00-17/2-2021) 10. veljače 2021. Bolesnici s aksijalnim i/ili perifernim SpA-om novačeni su s Odjela reumatologije Specijalne bolnice za medicinsku rehabilitaciju srca, pluća i reumatizma Thalassotherapia-Opatija Hrvatska od 10. veljače 2021. do 28. veljače 2023. godine, nakon obavljenoga kliničkoga reumatološkog pregleda i pregleda laboratorijskih nalaza. Kriteriji za uključivanje bili su bol u vratnoj kralježnici i dob od 18 do 80 godina. Kriteriji za isključenje bili su reumatoidni artritis, sistemske bolesti vezivnoga tkiva, imunodeficijencija, akutna infekcija, trudnoća, zloćudna bolest u posljednjih 5 godina, nekontrolirana šećerna bolest (glukoza u plazmi > 11 mmol/L), nekontrolirana arterijska hipertenzija (> 160/100 mmHg), akutni koronarni događaji, III. i IV. stupanj zatajenja srca prema razradbi New York Heart Associationa, IV. stupanj zatajenja bubrega, lezije jetara (ALT, AST i GGT tri ili više puta iznad gornje granice normale) kako bi se izbjegle značajne promjene u imunosnom sustavu osim SpA-a. Isključeni su i bolesnici s kongenitalnim/razvojnim poremećajima TMZ-a. Na temelju tih mjerila odabrana su 233 bolesnika sa SpA-om i oni su potpisali informirani pristanak za sudjelovanje i upućeni su liječniku dentalne medicine na klinički pregled TMZ-a. Ovo istraživanje u skladu je sa svim primjenjivim smjernicama kojima je svrha osigurati ispravno ponašanje i sigurnost sudionika, uključujući Helsinšku deklaraciju Svjetskoga medicinskog udruženja (Edinburgh, 2000.). Tijekom ove studije bolesnici nisu mijenjali redovitu terapiju, niti su uzimali dodatne tvari/lijekove (placebo).

Reumatološki pregled

Reumatolog je pregledao bolesnike i dijagnosticirao SpA prema mjerilima razradbe ASAS-a (The Assessment of SpondyloArthritis International Society) (26). Zabilježeni su sljedeći podatci: dob (godine), spol, indeks tjelesne mase (ITM, kg/m^2), trajanje SpA-a, dob početka SpA-a (godine) te trenutačna terapija prema elektroničkome bolničkom informacijskom sustavu (WinBis, IN2 d.o.o., Zagreb, Hrvatska). Trenutačna aktivnost SpA-a procijenjena je korištenjem ASDAS-a (Ankylosing Spondylitis Disease Activity Score), bolesnikove samoprocijenjene jakosti aksijalnih i perifernih bolova, aktivnosti SpA-a (vizualna analogna ljestvica [VAS] od 1 do 10) (27) i ukupnih tjelesnih bolova (vizualna analogna ljestvica od 1 do 100 mm). BASDAI (Bath Ankylosing Spondylitis Disease Activity Indeks) korišten je za procjenu bolova u vratu (28). Izračunat je indeks aktivnosti bolesti za psorijatični artritis (DAPSA) (29). Zabilježili smo i poteškoće bolesnika u obavljanju svakodnevnih aktivnosti (VAS 1-10).

Laboratorijske analize

Laboratorijske analize obavljene su na temelju jednog uzorka periferne venske krvi od 12 mL iz kubitalne vene. Broj eritrocita, leukocita i trombocita, te hematokrit i koncentracija hemoglobina, analizirani su hematološkim anali-

analyzed using a hematology analyzer (Sysmex XN-550, Kobe, Japan). C-reactive protein, serum alpha-amylase, and anti-streptolysin O titer (ASTO) were measured using an automatic biochemical analyzer (Cobas Pro, Roche Diagnostics, and Boehringer Mannheim).

Imaging methods

Patients underwent MRI of the sacroiliac joints and thoracolumbar transition zone, according to the clinical presentation of the disease (Siemens Avanto 1.5 T Syngo MR B17, Erlanger, Germany). MRI was performed without a radiographic contrast agent, following the ASAS protocol (26). Ultrasound (ultrasonic device and linear probe of 20 kHz, Loggic e, General Electric, Niskayuna, New York, USA), X-ray [tube (Siemens, Wuxi, China), table (Siemens, Munich, Germany)] or MRI (Siemens Avanto 1.5 T Syngo MR B17) were used to assess the peripheral form of SpA.

Examination of temporomandibular joints (TMJs)

Clinical examination of the TMJs was performed by a dentist according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD protocol) (9**).** The results were recorded in the DC/TMD form and analyzed (30). Axis I is a form for clinical examination, and Axis II consists of a series of self-administrated instruments that assess functional, behavioral and psychosocial status. The diagnosis was established by integrating the findings from Axis I and Axis II, following the diagnostic algorithms for "Pain associated with TMJ and headache" and "Joint disorders and degenerative joint disorders" (31).

Statistical analyses

Statistical analyses were performed using Statistica 14.0.0.15 (TIBCO, Software Inc., Palo Alto, California, USA). All numerical parameters were normally distributed. Differences among three groups for continuous scales were analyzed using one-way analysis of variance (ANOVA). Tukey's post-hoc test analyzed differences between any two of three researched groups, and Bonferroni correction served to exclude a false positive result. Categorical data were analyzed using Chi-square tests for multiple independent samples with Yates correction, which improved the accuracy of the p-value obtained with Chi-square tests. In the case of a statistically significant difference obtained by the Yates correction between two groups of categorical data, the significance was checked using the Fischer's exact test, which also precisely determines the P value. Variables on continuous scales were presented as means and 95% of confidence intervals, while categorical variables were presented as counts and percentages.

Results

Allocation of patients in the investigation groups

A flowchart depicting the recruitment and distribution of patients with SpA is provided (Figure 1).

Following clinical examination of the TMJs in 233 patients with SpA using the DC/TMJ protocol, 33 patients

zatorom (Sysmex XN-550, Kobe, Japan). C-reaktivni protein, α-amilaza u serumu i titar antistreptolizina O (ASTO) mjereni su s pomoću automatskoga biokemijskog analizatora (Cobas Pro, Roche Diagnostics, Boehringer Mannheim).

Metode snimanja

Bolesnici su bili na magnetskoj rezonanciji (MR) sakroilijačnih zglobova i područja prijelaza prsne (torakalne) kralježnice u slabinsku, prema kliničkoj slici bolesti (Siemens Avanto 1.5 T Syngo MR B17, Erlanger, Njemačka). MR je učinjen bez radiografskoga kontrastnog sredstva, prema protokolu ASAS (26). Dijagnostika ultrazvukom (ultrazvučni uređaj i linearna sonda od 20 kHz, Loggic e, General Electric, Niskayuna, New York, SAD), rendgenskim snimanjem [cijev (Siemens, Wuxi, Kina), stol (Siemens, München, Njemačka)] ili MR (Siemens Avanto 1,5 T Syngo MR B17) koristili su se za procjenu perifernoga oblika SpA-a.

Pregled temporomandibularnih zglobova

Klinički pregled TMZ-a obavila je doktorica dentalne medicine prema protokolu Dijagnostički kriteriji za temporomandibularne poremećaje (DK/TMP) (9). Rezultati su zabilježeni u DK/TMP obrascu i analizirani (30). Os I je obrazac za klinički pregled, a Os II sastoji se od niza instrumenata koji ispunjava bolesnik uz pomoć ispitivača, a tim se obrascem procjenjuje ponašanje te psihosocijalno i funkcijsko stanje. Dijagnoza se postavlja objedinjavanjem tih dvaju nalaza, slijedeći dijagnostičke algoritme za bolne i intrakapsularne TMP-ove (31).

Statističke analize

Statističke analize obavljene su u programu Statistica 14.0.0.15 (TIBCO, Software Inc., Palo Alto, Kalifornija, SAD). Svi numerički parametri bili su normalno raspoređeni. Razlike između triju skupina za kontinuirane ljestvice analizirane su jednosmjernom analizom varijance (ANOVA). Tukeyjevim post-hoc testom analizirane su razlike između bilo kojih dviju od triju istraživanih skupina, a Bonferronijeva korekcija služila je za isključivanje lažno pozitivnog rezultata. Kategorički podatci analizirani su korištenjem Hi-kvadrat testa za više neovisnih uzoraka s Yatesovom korekcijom, što je poboljšalo točnost p-vrijednosti dobivene Hi-kvadrat testom. U slučaju statistički značajne razlike dobivene Yatesovom korekcijom između dviju skupina kategoričkih podataka, značajnost je provjerena Fischerovim egzaktnim testom koji također precizno određuje P vrijednost. Varijable na kontinuiranim ljestvicama prikazane su kao srednje vrijednosti i 95-postotni interval pouzdanosti, a kategoričke varijable kao brojevi i postotci.

Rezultati

Raspodjela bolesnika u skupine

Dijagram toka pokazuje odabir i raspodjelu bolesnika sa SpA-om (slika 1.).

Nakon kliničkoga pregleda TMZ-a, 233 bolesnika sa SpA-om korištenjem DK/TMP protokola, 33 bolesnika s

with disorders related to muscle and joint pain and headache without ID were excluded from the study. The remaining 200 patients diagnosed as ReA (n = 62), PsA (n = 57), HLA-B27+ SpA (n = 33), enteropathic SpA (n = 8), and undifferentiated SpA (n = 40) remained in the research. Among these, 114 patients (57% of the 200) were diagnosed with one or more IDs, including disc displacement with reduction (n = 77), disc displacement with reduction and intermittent locking (n = 10), disc displacement without reduction and with limited opening (n = 9), disc displacement without reduction and without limited opening (n = 3), and degenerative joint disease (n = 41). Of these 114 patients with ID, 48 also had concurrent pain associated with TMJ and headache, which included local myalgia (n = 3), myofascial pain (n = 17), myofascial pain with spreading (n = 14), and headache attributed to TMDs (n = 14). Among patients with ID, 64patients (56%) felt pain of articular origin according to the DC/TMD protocol and they were classified as symptomatic ID in this research. Patients with ID of TMJ without articular pain, 50 (44%) were considered asymptomatic regardless of whether they experienced a joint's sounds. Healthy TMJs were found in 86 patients with SpA (43 %), representing the control group. Therefore, 200 patients with SpA were categorized into three groups based on the clinical examination of the TMJs as follows: patients with symptomatic ID (group A), patients with asymptomatic ID (group B), and patients with healthy TMJs (group C or controls).

poremećajima povezanima s bolovima u mišićima i zglobovima te glavoboljom bez IK TMP-a, isključeni su iz istraživanja. Preostalih 200 s dijagnozom ReA-a (n = 62), PsA-a (n = 57), *HLA-B27* + SpA (n = 33), enteropatskog SpA-a (n = 8) i nediferenciranog SpA-a (n = 40) zadržano je u istraživanju. Među njima je kod njih 57 % (114 od 200) dijagnosticiran jedan ili više IK TMP-ova, uključujući pomak diska s redukcijom (n = 77), pomak diska s redukcijom i povremenim kočenjem (n = 10), pomak diska bez redukcije i s ograničenim otvaranjem (n = 9), pomak diska bez redukcije i bez ograničenog otvaranja (n = 3) i degenerativnu bolest zgloba (n = 41). Od navedenih 114 bolesnika s IK TMP-om, 48 je također imalo istodobne bolove povezane s TMZ-om i glavobolje, što je uključivalo lokalnu mijalgiju (n = 3), miofascijalnu bol (n = 17), prenesenu miofascijalnu bol (n = 14) i glavobolju koja se može pripisati TMP-u (n = 14). Među bolesnicima s IK TMP-om njih 64 (56 %) osjećalo je bolove zglobnoga podrijetla (artralgija) prema protokolu DK/TMP te su u ovom istraživanju razvrstani u skupinu simptomatskih IK TMP-a. Bolesnici (n = 50) s IK TMP-om bez artralgije (44 %) smatrali su se asimptomatskima bez obzira na to jesu li im se pojavljivali zvukovi u zglobu. Zdravi TMZ-ovi pronađeni su kod 86 bolesnika sa SpA-om (43 %) i oni su bili kontrolna skupina. Stoga je 200 bolesnika sa SpA-om svrstano u tri skupine na temelju kliničkoga pregleda TMZ-a kako slijedi: bolesnici sa simptomatskim IK TMP-om (skupina A), bolesnici s asimptomatskim IK TMP-om (skupina B) i bolesnici sa zdravim TMZ-om (skupina C ili kontrola).

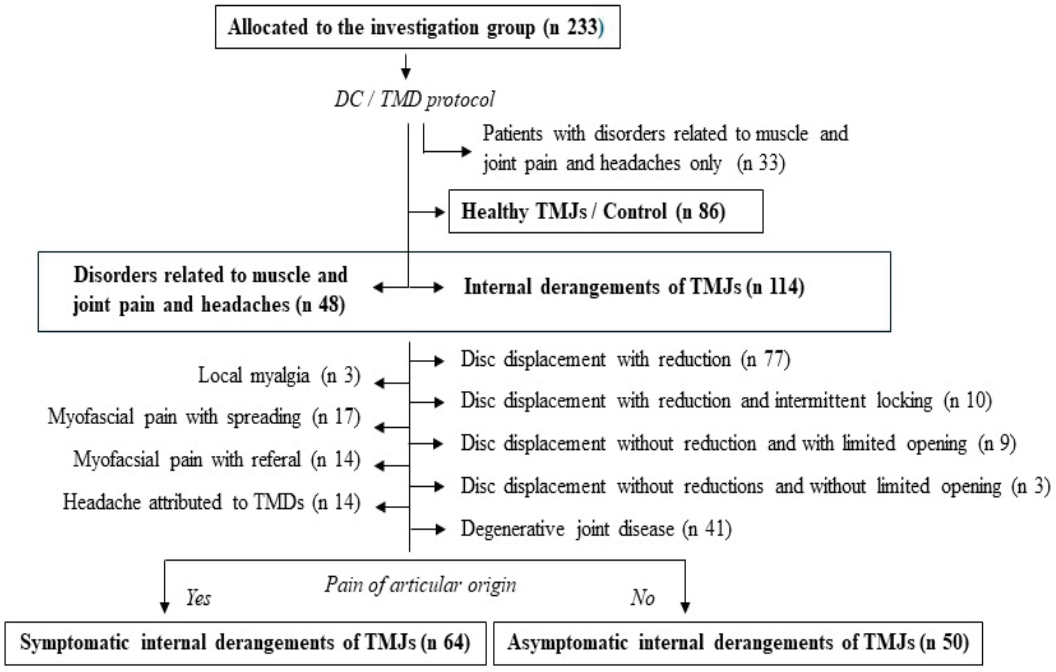

Figure 1 Recruitment and allocation of patients with spondyloarthritis (SpA) to the assessment groups. Abbreviations: ASAS – The Assessment of Spondyloarthritis International Society; DC/TMD – Diagnostic Criteria for Temporomandibular Disorders; n – number of patients; TMDs – temporomandibular disorders; TMJs – temporomandibular joints.
Slika 1. Odabir i raspodjela bolesnika sa spondiloartritisom (SpA) u skupine za procjenu. Kratice: DK/TMP – dijagnostički kriteriji za temporomandibularne poremećaje; IK TMP – intrakapsularni temporomandibularni poremećaj; n – broj bolesnika; TMP – temporomandibularni poremećaj; TMZ-ovi – temporomandibularni zglobovi

Radiological findings and therapy of patients with SpA

Table 1 shows radiologic findings and therapies for SpA. Exacerbation of axial SpA was most common in patients with asymptomatic ID of TMJ (74%), significantly higher than in the control group (52.3%; P= 0.0401 Chi-square test; P = 0.0209 Yates-corrected Chi-square test; P = 0.0098, Fisher's exact test) but not significantly different from those with symptomatic ID. Ankylosis was also more prevalent in patients with asymptomatic ID (24%) compared to 8.13% in the control (P = 0.0319 Chi-square test; P = 0.0206, Yates-corrected Chi-square test; P = 0.0113, Fisher's exact test). The proportion of patients with peripheral SpA did not differ across the groups, although peripheral SpA was expressed in over 80% of patients, primarily due to enthesitis. Patients in all three research groups received comparable treatments, including non-steroidal anti-inflammatory drugs, sulfasalazine, and methotrexate, or were without therapy at the time of recruitment in the study.

Radiološki nalazi i terapija bolesnika sa spondiloartritisom

U tablici 1. su radiološki nalazi i terapija za SpA. Pogoršanje aksijalnoga SpA-a bilo je najčešće kod bolesnika s asimptomatskim IK TMP-om (74 %), znatno više nego u kontrolnoj skupini (52,3 %; P = 0,0401 Hi-kvadrat test; P = 0,0209 Yates-korigirani Hi-kvadrat test; P = 0,0098, Fisherov egzaktni test), ali nije se razlikovalo značajno od bolesnika sa simptomatskim IK TMP-om. Ankiloza je također bila češća kod bolesnika s asimptomatskim IK TMP-om (24 %) u usporedbi s 8,13 % u kontrolnoj skupini (P = 0,0319 Hi-kvadrat test; P = 0,0206, Yates-ispravljeni Hi-kvadrat test; P = 0,0113, Fisherov egzaktni test). Udio bolesnika s perifernim SpA-om nije se razlikovao među skupinama, iako je periferni SpA bio izražen kod više od 80 % bolesnika, uglavnom zbog entezitisa. Bolesnici u svim trima istraživanim skupinama imali su usporedivu terapiju, uključujući nesteroidne protuupalne lijekove, sulfasalazin i metotreksat, ili su bili bez terapije kada su uključeni u istraživanje.

Table 1 Radiological findings in patients with spondyloarthritis (SpA) and medical treatment of spondyloarthritis (SpA). Differences among groups of patients with symptomatic internal derangement ((ID) of temporomandibular joint (TMJ) (group A), asymptomatic ID of TMJ (group B) and control (group C) were analyzed using tests for comparing multiple independent samples (Chi-square test with Yates correction and Fisher exact one-tailed test). Statistical significance (P) between group A and group C ([a]); group B and group C ([b]); Yates correction ([y])

Tablica 1. Radiološki nalazi bolesnika sa spondiloartritisom (SpA-om) i medicinsko liječenje SpA-a. Razlike između skupina bolesnika sa simptomatskim intrakapsularnim temporomandibularnim poremećajem (IK TMP) (skupina A), asimptomatskim IK TMP-om (skupina B) i kontrola (skupina C) analizirane su s pomoću testova za usporedbu više neovisnih uzoraka (Hi-kvadrat test s Yatesovom korekcijom i Fisherovim egzaktnim jednostranim testom). Statistička značajnost (P) između skupine A i skupine C ([a]); skupine B i skupine C ([b]); Yatesova korekcija ([y]).

Patients with SpA • Bolesnici sa SpA-om	Group A • Skupina A N/64 (%)	Group B • Skupina B N/50 (%)	Group C • Skupina C N/86 (%)	Chi-square test for multiple independent samples • $\chi 2$ test za više nezavisnih uzoraka	Chi-square test Yates correction • $\chi 2$ test Yatesova korekcija	Fisher's exact test • Fisherov egzaktni test
Radiological findings in patients with SpA • Radiološki nalazi				**P levels**		
Axial type • Aksijalni oblik SpA-e	42 (65.6)	40 (80.0)	54 (62.8)	0.1029		
Exacerbation of axial SpA • Pogoršanje aksijalnog oblika SpA-e	36 (56.2)	37 (74.0)	45 (52.3)	0.0401	[b]0.0127; [y]0.0209	[b]0.0098
Vertebral corner inflammatory lesion • Upalna lezija vertebralnog kuta	10 (15.62)	13 (26.0)	11 (12.8)	0.1329		
Symmetric BM edema of SIJs • Simetrični edem koštane srži SIZ	16 (25.0)	10 (20.0)	15 (17.4)	0.5230		
Asymmetric BM edema of SIJs • Asimetrični edem koštane srži SIZ	18 (28.12)	24 (48.0)	30 (34.9)	0.0884		
Structural changes of SIJs • Strukturne promjene SIZ-a	33 (51.6)	30 (60.0)	49 (57.0)	0.5230		
Erosion • Erozija	28 (43.8)	22 (44.0)	40 (46.5)	0.9324		
Fat metaplasia • Masna metaplazija	15 (23.4)	15 (30.0)	33 (38,4)	0,1450		
Ankylosis • Ankiloza	8 (12.5)	12 (24.0)	7 (8.13)	0.0319	[b]0.0101;[y]0.0206	[b]0.0113
Peripheral type • Periferni oblik SpA-e	52 (81.0)	44 (88.0)	77 (89.5)	0.3190		
Arthritis • Artritis	40 (62.5)	32 (64.0)	57 (66.3)	0.8886		
Enthesitis • Entezitis	45 (70.3)	41 (82.0)	59 (68.6)	0.2153		
Dactylitis • Daktilitis	7 (10.9)	7 (14.0)	7 (8.13)	1		
Axial and peripheral type • Aksijalni i periferni oblik	31 (48.43)	34 (68)	43 (50)	0.07		
Drugs for treatment of SpA • Lijekovi za liječenje SpA-e						
Nihil • Ništa	14 (21.78)	13 (26)	16 (18.6)	0.5968		
NSAIDs • NSAIL	47 (73.43)	35 (70)	65 (75,6)	0.7765		
Sulfasalazine • Sulfasalazin	17 (26.56)	20 (40.0)	22 (25.6)	0.1694		
Methotrexate • Metotreksat	6 (9.37)	11 (22.0)	17 (19.8)	0.1360		

Abbreviations: BM - bone marrow; NSAIDs - Non-Steroidal Anti-Inflammatory Drugs; SIJs - sacroiliac joints. •
Kratice: NSAIL – nesteroidni protuupalni lijekovi; SIZ – sakroilijakalni zglobovi; SpA – spondiloartritis

Clinical characteristics of patients and activity of SpA

Figure 2 and Figure 3 show the clinical characteristics of the patients and their SpA activity. Women were more represented than men in the symptomatic and asymptomatic ID groups (P < 0.0001), as well as in the control group (P = 0.0006) as analyzed using Fisher's exact test (Figure 2A, 2B, and 2C, respectively). Age (Figure 2D), BMI (Figure 2E), and SpA duration (Figure 2F) were comparable across the groups. Patients with symptomatic ID were significantly younger at SpA onset than those in the control group (Figure 2G, P = 0.015, Bonferroni adjustment of P value obtained by One-way ANOVA and Tukey post-hock test).

Kliničke značajke bolesnika i aktivnost spondiloartritisa

Slika 2. i slika 3. prikazuju kliničke značajke bolesnika i aktivnost njihova SpA-a. Žene su bile zastupljenije od muškaraca u skupinama sa simptomatskim i asimptomatskim IK TMP-om (P < 0,0001) te u kontrolnoj skupini (P = 0,0006), kako je analizirano Fisherovim egzaktnim testom (slika 2.A, 2.B, odnosno 2.C). Dob (slika 2.D), ITM (slika 2.E) i trajanje SpA-a (slika 2.F) bili su usporedivi među grupama. Bolesnici sa simptomatskim IK TMP-om bili su znatno mlađi na početku SpA-a od onih u kontrolnoj skupini (slika 2.G, P = 0,015, Bonferronijeva prilagodba P vrijednosti dobivena jednosmjernom ANOVA-om i Tukeyjevim post-hoc testovima).

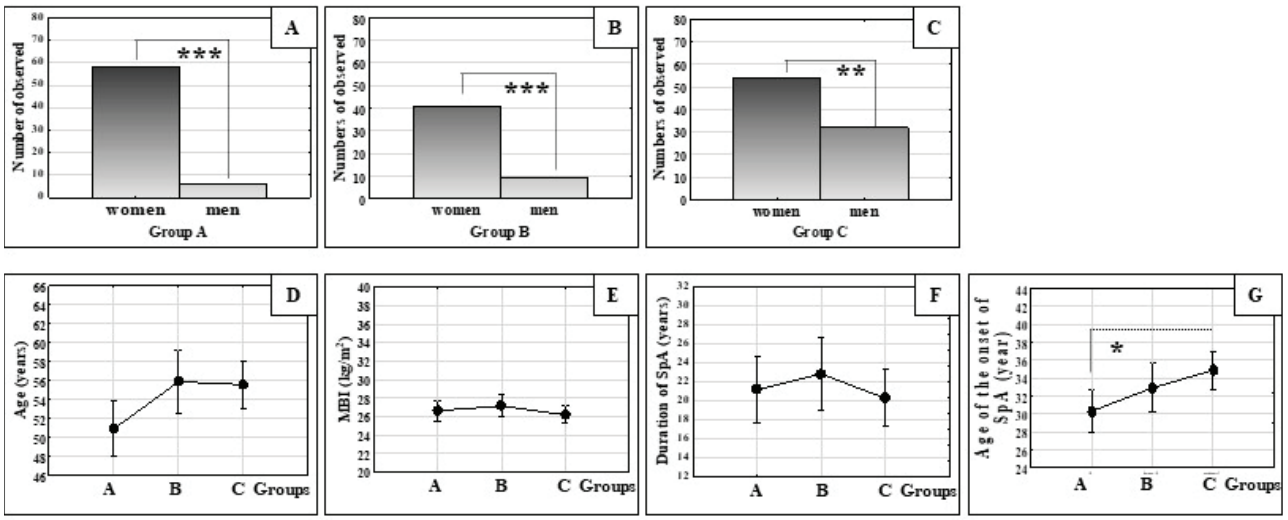

Figure 2 Clinical characteristics of patients with spondyloarthritis (SpA) suffering from symptomatic internal derangement (ID) of temporomandibular joint (TMJ) (group A), asymptomatic ID of TMJ (group B), and control (group C). Bar graphs show (A) sex distribution in group A, (B) sex distribution in group B, and (C) sex distribution in group C. The line graph displays (D) age, (E) body mass index (BMI), (F) duration of SpA, and (G) age of the onset of SpA in groups A, B and C. · Mean, and I mean ± 0.95 confidence interval. Levels of statistical significance (P): *0.015 (Bonferroni adjustment of P value obtained by One-way ANOVA and Tukey post-hock test); ** 0.0006 and *** < 0.0001 (Fischer exact test). • Mean, and **I** mean ± 0.95 confidence interval.

Slika 2. Kliničke značajke bolesnika sa spondiloartritisom (SpA) i simptomatskim intrakapsularnim temporomandibularnim poremećajem (IK TMP) (skupina A), asimptomatskim IK TMP-om (skupina B) i kontrola (skupina C). Stupčasti dijagrami prikazuju (A) spolnu raspodjelu u skupini A, (B) spolnu raspodjelu u skupini B i (C) spolnu raspodjelu u skupini C. Linijski grafikon prikazuje (D) dob, (E) indeks tjelesne mase (ITM), (F) trajanje SpA-a i (G) dob početka SpA-a u skupinama A, B i C. Razine statističke značajnosti (P): *0,015 (Bonferronijeva prilagodba P vrijednosti dobivena je jednosmjernom ANOVA-om i Tukeyjevim post-hoc testovima); ** 0,0006 i *** < 0,0001 (Fischerov egzaktni test). • Srednja vrijednost i srednje vrijednosti ± 0,95 intervala pouzdanosti.

ASDAS-CRP levels were higher in patients with symptomatic (P = 0.0008) and asymptomatic (P = 0.002) ID groups compared to the control (Figure 3A). BASDAI (P = 0.002) and DAPSA (P = 0.0004) scores were higher in patients with symptomatic ID compared to control (Figure 3B and Figure 3C, respectively). Patients with symptomatic ID had greater difficulties in performing total daily activities (P = 0.049) than the control group (Figure 3D). Patients' self-estimated SpA activity was significantly higher in both symptomatic (P = 0.000004) and asymptomatic (P = 0.002) ID groups than in the control (Figure 3E). Total body pain (Figure 3F) was greater in patients with symptomatic ID than in the control (P = 0.0008). Axial pain was greater in both the symptomatic (P = 0.006) and asymptomatic ID groups (P = 0.0004) compared to controls, averaging approximately 5 on

Razine ASDAS-CRP-a bile su više kod bolesnika sa simptomatskim (P = 0,0008) i asimptomatskim (P = 0,002) IK TMP-om u usporedbi s kontrolom (slika 3.A). Rezultati BASDAI-ija (P = 0,002) i DAPSA-e (P = 0,0004) bili su viši kod bolesnika sa simptomatskim IK TMP-om u usporedbi s kontrolom (slika 3.B, odnosno slika 3.C). Bolesnici sa simptomatskim IK TMP-om imali su veće poteškoće u obavljanju ukupnih dnevnih aktivnosti (P = 0,049) nego kontrolna skupina (slika 3.D).

Bolesnikova samoprocjena aktivnosti SpA-a bila je značajno viša u simptomatskoj (P = 0,000004) i asimptomatskoj (P = 0,002) skupini s IK TMP-om nego u kontrolnoj (slika 3.E). Ukupni tjelesni bolovi (slika 3.F) bili su snažniji kod bolesnika sa simptomatskim IK TMP-om nego u kontrolnoj skupini (P = 0,0008). Aksijalni bolovi bili su snažniji u simp-

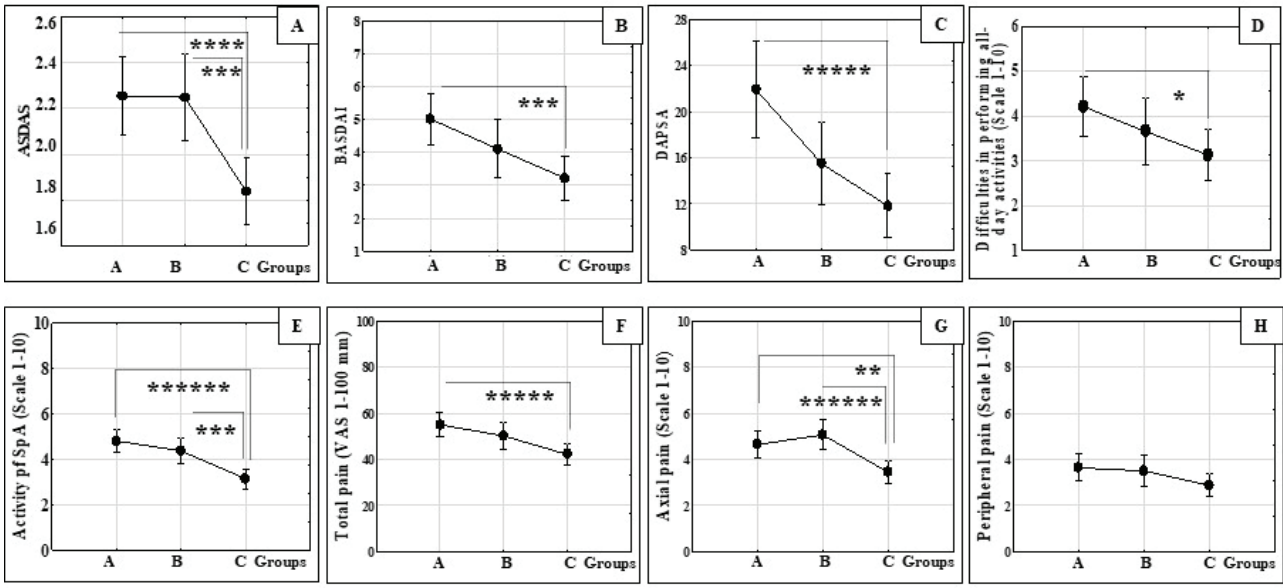

Figure 3 Clinical parameters of spondyloarthritis (SpA) activity in patients with symptomatic internal derangement (ID) of temporomandibular joint (TMJ) (group A), asymptomatic ID of TMJ (group B) and control (group C). Graphs show (A) ASDAS - Ankylosing Spondylitis Disease Activity Score; (B) BASDAI - Bath Ankylosing Spondylitis Disease Activity Index; (C) DAPSA - Disease Activity Index in Psoriatic Arthritis; (D) Difficulties in performing all day activities (Scale 1-10); (E) patients' self-estimated activity of SpA on a visual analogue scale (VAS); (F) VAS for overall pain; (G) VAS for axial pain and (H) VAS for peripheral pain in groups A, B, and C. Levels of statistical significances (P): * 0.049; ** 0.006; *** 0.002; **** 0.0008; ***** 0.0004 and ****** 0.000004 (Bonferroni test correction of P values obtained by One-way ANOVA and Tukey post-hoc test). • Mean, and I mean ± 0.95 confidence interval.

Slika 3. Klinički parametri aktivnosti spondiloartritisa (SpA) kod bolesnika sa simptomatskim intrakapsularnim temporomandibularnim poremećajem (IK TMP) (skupina A), asimptomatskim IK TMP-om (skupina B) i kontrola (skupina C). Grafikoni prikazuju (A) ASDAS (engl. Ankylosing Spondylitis Disease Activity Score); (B) BASDAI (engl. Bath Ankylosing Spondylitis Disease Activity Index); (C) DAPSA-u (engl. Disease Activity Index in Psoriatic Arthritis); (D) Poteškoće u obavljanju cjelodnevnih aktivnosti; (E) bolesnikovu samoprocijenjenu aktivnost SpA-e na vizualnoj analognoj ljestvici (VAS); (F) VAS za ukupne bolove; (G) VAS za aksijalne bolove i (H) VAS za periferne bolove u skupinama A, B i C. Razine statističke značajnosti (P): * 0,049; ** 0,006; *** 0,002; **** 0,0008; ***** 0,0004 i ****** 0,000004 (Bonferronijev test korekcija P vrijednosti dobivenih jednosmjernom ANOVA-om i Tukeyjevim post-hoc testovima). • Srednja vrijednost, I srednja vrijednost ± 0,95 interval pouzdanosti.

a scale of 0 to 10 (Figure 3G). VAS scores for peripheral pain did not differ significantly across groups (Figure 3H).

Laboratory characteristics of patients with SpA

Figure 4 shows laboratory characteristics of patients with SpA**.** Erythrocyte counts were comparable across groups (Figure 4A). Hemoglobin concentration was lower (P = 0.017) in patients suffering from symptomatic ID (136 g/L [133 -138], mean [0.95 Confidence Interval]) when compared with control (141 g/L [139 -143], Figure 4B). Hematocrit was lower in patients with symptomatic ID (0.4 % [0.4-0.41]) and asymptomatic ID (0.4 % [0.39-0.44]) when compared with control (0.42 [0.42 - 0.43], P = 0.007, Figure 4C). Platelet counts were significantly higher (P = 0.017) in patients with symptomatic ID (274 x 10^9/L [258 x 10^9 - 290 x 10^9]) when compared with control (248 x 10^9/L [237 x 10^9 - 260 x 10^9], Figure 4D). Leukocyte counts (Figure 4E) and CRP levels (Figure 4F) were within normal ranges and did not significantly differ across the groups. Serum concentration of alpha-amylase was significantly higher (P = 0.017) in patients with symptomatic ID (76 IU/L [66 - 85]) than in the control group (62 IU/L [57 - 67]), (Figure 4G). ASTO was significantly higher (P = 0.049) in patients with symptomatskim (P = 0,006) i asimptomatskim skupinama s IK TMP-om (P = 0,0004) u usporedbi s kontrolom i iznosili su u prosjeku približno 5 na ljestvici od 0 do 10 (slika 3.G). VAS rezultati za perifernu bol nisu se značajno razlikovali među skupinama (slika 3.H).

Laboratorijske značajke bolesnika sa spondiloartritisom

Na slici 4. laboratorijske su značajke bolesnika sa SpA-om. Brojnost eritrocita bila je usporediva među skupinama (slika 4.A). Koncentracija hemoglobina bila je niža (P = 0,017) kod bolesnika koji su patili od simptomatskoga IK TMP-a (136 g/L [133 – 138], srednja vrijednost [0,95 intervala pouzdanosti]) u usporedbi s kontrolom (141 g/L [139 – 143], slika 4B). Hematokrit je bio niži kod bolesnika sa simptomatskim IK TMP-om (0,4 % [0,4 – 0,41]) i asimptomatskim IK TMP-om (0,4 % [0,39 – 0,44]) u usporedbi s kontrolom (0,42 [0,42 – 0,43], P = 0,007, slika 4.C). Broj trombocita bio je značajno veći (P = 0,017) kod bolesnika sa simptomatskim IK TMP-om (274 x 10^9/L [258 x 10^9 – 290 x 10^9]) u usporedbi s kontrolom (248 x 10^9/L [237 x 10^9 – 260 x 10^9], slika 4.D). Broj leukocita (slika 4.E) i koncentracija CRP-a (slika 4.F) bili su unutar normalnih raspona i nisu se značajno razlikovali među skupinama. Koncentracija α-amilaze u serumu bila je značajno viša (P = 0,017) kod bolesnika sa simptomatskim IK TMP-om (76 IU/L [66 – 85])

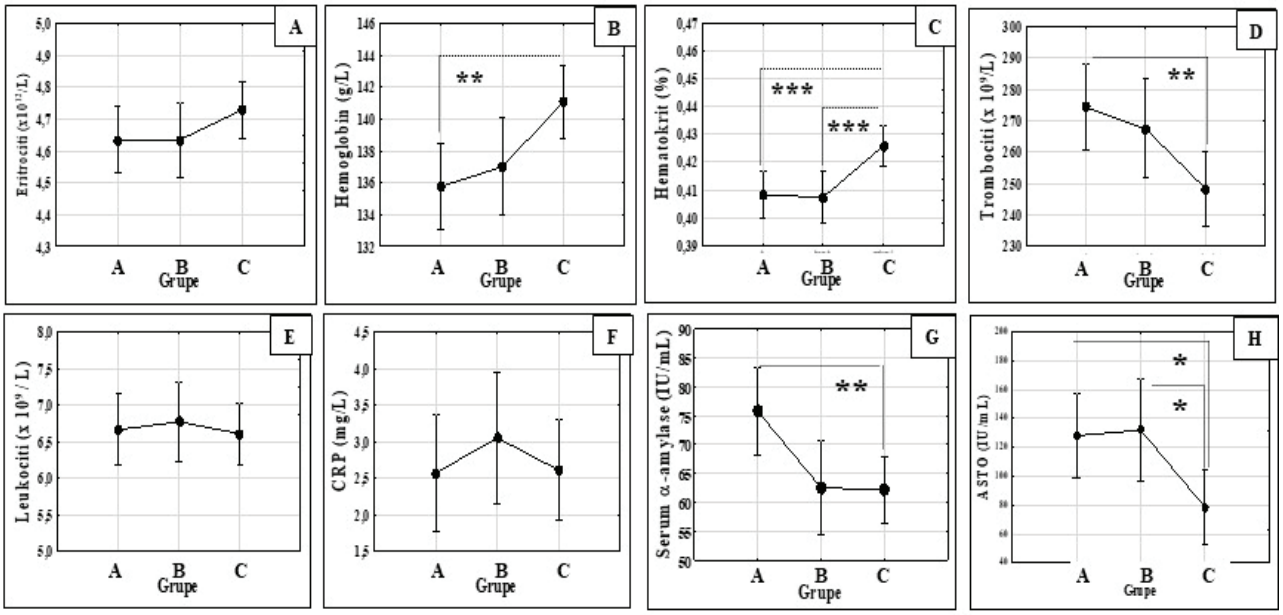

Figure 4 Laboratory parameters of activity of spondyloarthritis (SpA) in patients with symptomatic internal derangement (ID) of temporomandibular joint (TMJ) (group A), asymptomatic ID of TMJ (group B) and control (group C). Graphs show (A) erythrocyte count, (B) hemoglobin concentration, (C) hematocrit, (D) platelet count, (E) leukocyte count, (F) C-reactive protein (CRP), (G) serum alpha-amylase, and (H) antistreptolysin O titre (ASTO) in groups A, B, and C. Levels of statistical significance (P): * 0.049; ** 0.017; *** 0.007 (Bonferroni test correction of P values obtained using One-way ANOVA and Tukey post-hock test). • Mean, and I mean ± 0.95 confidence interval.

Slika 4. Laboratorijski parametri aktivnosti spondiloartritisa (SpA) kod bolesnika sa simptomatskim intrakapsularnim temporomandibularnim poremećajem (IK TMP) (skupina A), asimptomatskim IK TMP-om (skupina B) i kontroli (skupina C). Grafikoni prikazuju (A) broj eritrocita, (B) koncentraciju hemoglobina, (C) hematokrit, (D) broj trombocita, (E) broj leukocita, (F) C-reaktivni protein (CRP), (G) α-amilazu u serumu i (H) titar antistreptolizina O (ASTO) u skupinama A, B i C. Razine statističke značajnosti (P): * 0,049; ** 0,017; *** 0,007 (korekcija P vrijednosti Bonferronijeva testa dobivena korištenjem jednosmjerne ANOVA-e i Tukeyjev post-hoc testova). • Srednja vrijednost, I srednja vrijednost ± 0,95 interval pouzdanosti.

tomatic ID (128 IU/mL [93 - 162]) and asymptomatic ID (132 IU/mL [88 - 176]) than in the controls (79 IU/mL [61 - 96], Figure 4H).

Discussion

Our study demonstrated for the first time that patients with SpA who suffer from IDs have exacerbated axial disease, as indicated by radiologic findings of the sacroiliac joints, laboratory findings, and rheumatological examination. Women were more represented than men, likewise in some earlier studies (11,12). Disc displacement with reduction was the most common ID in patients with SpA, as well as in patients without SpA of appropriate age (11). Symptomatic ID presents a large burden for patients, consistent with recent data from Syrmou et al. (29) and Vrbanović et al. (11). Notably, in addition to symptomatic ID, many patients with asymptomatic ID were diagnosed using the DC/TMD protocol, particularly in patients with exacerbation of axial SpA and structural changes of the sacroiliac joints compared to controls, regardless of SpA duration. This finding aligns with the increased risk of developing TMDs in patients with r-axSpA (8). A recently published meta-analysis by Brazilian researchers also reported a higher prevalence of asymptomatic TMDs in patients with axSpA (33). This is consistent with

nego u kontrolnoj skupini (62 IU/L [57 – 67], slika 4.G). ASTO je bio značajno viši (P = 0,049) kod bolesnika sa simptomatskim IK TMP-om (128 IU/mL [93 – 162]) i asimptomatskim IK TMP-om (132 IU/mL [88 - 176]) nego u kontrolnoj skupini (79 IU/mL [61 – 96], slika 4.H).

Rasprava

Naše istraživanje prvi je put pokazalo da bolesnici sa SpA-om koji pate od IK TMP-a imaju pogoršanu aksijalnu bolest, na što upućuju radiološki nalazi sakroilijačnih zglobova, laboratorijski nalazi i reumatološki pregled. Žene su bile zastupljenije od muškaraca, kao i u ranijim istraživanjima (11, 12). Pomak diska (pločice) s redukcijom bio je najčešći IK TMP kod bolesnika sa SpA-om, te onih bez SpA-a odgovarajuće dobi (11). Simptomatski IK TMP veliko je zdravstveno opterećenje za bolesnike, u skladu s nedavno objavljenim podatcima Syrmoua i suradnika (29) i Vrbanovića i suradnika (11). Značajno, uz simptomatski IK TMP, mnogi bolesnici s asimptomatskim IK TMP-om dijagnosticirani su korištenjem protokola DK/TMP, osobito kod onih s pogoršanjem aksijalnog SpA-a i strukturnim promjenama sakroilijačnih zglobova u usporedbi s kontrolama, bez obzira na trajanje SpA-a. Taj je nalaz u skladu s povećanim rizikom od pojave TMP-a kod bolesnika s r-axSpA-om (8). U nedavno objavljenoj metaanalizi brazilski su istraživači također izvijestili o većoj prevalenciji asimptomatskih TMP-ova kod bo-

the hypothesis that asymptomatic ID is not clinically manifested in patients with SpA, although the same immunepathogenetic mechanism likely exists in the underlying disease, as seen in patients with symptomatic TMDs where the disease presents with all its main symptoms (34). Gut dysbiosis and frequent subclinical chronic intestinal inflammation underlie various clinical manifestations of SpA (35), including TMDs (36). Accordingly, increased serum alpha-amylase might reflect the greater proliferative capacity of small intestine epithelial cells (37), thus indicating more pronounced inflammation in patients with symptomatic than in asymptomatic ID and controls. Thus, osteoarthritis (10,38) and, particularly, disc displacement in the TMJ (19), supported by radiological findings, can be completely asymptomatic, probably due to the lower degree of inflammation and owing to the TMJ's large compensatory mechanisms (19,32).

MRI is the "gold standard" in diagnosis of ID of TMJs (12). In this study, MRI of the TMJs in the patients with asymptomatic ID was not performed, as current clinical practice often assumes that such symptoms are not severe enough to impact the patient significantly. Additionally, MRI is an expensive, time-consuming procedure performed by highly trained specialists that represents an economic burden on the community. Symptomatic ID in this investigation was diagnosed clinically using the validated Axis I protocol of the DC/TMD, which has 97% specificity and 80% sensitivity for detecting painful TMDs (9, 5). This is consistent with the recruitment of patients in a recently published meta-analysis based on clinical and/or radiographic evidence of TMDs (33). The high specificity and sensitivity of the DC/TMD protocol facilitate the diagnosis of symptomatic ID (11) and the diagnosis of SpA around the age of 30 years, which is significantly earlier compared to patients with intact TMJs. This aligns with the typical onset age for painful axial SpA (39), as pain, especially chronic pain in TMJs, often prompts young adults to seek medical attention (7,11,15). In contrast, patients with asymptomatic ID did not experience pain in the TMJs, likely explaining why their age of SpA onset did not differ significantly from that of the control group. Thus, ID of TMJs can progress asymptomatically for some time, remaining unrecognized as part of SpA and, therefore, seems to be inadequately treated, although it can be visualized by MRI (12). This can facilitate ID progression and the development of r-axSpA. Indeed, clinical parameters reflecting SpA activity, particularly markers of axial disease such as ASDAS-CRP (27), were elevated in both asymptomatic and symptomatic IDs compared with controls, indicating an equal burden in terms of health and quality of life in both patient groups. It is well-established (23) and recently confirmed (40) that psoriatic changes in painful TMJs show consequences of chronic inflammation (erosion) and joint effusion as a sign of acute inflammation on MRI, which is consistent with higher DAPSA scores in patients with symptomatic ID in this investigation. Patients with symptomatic and asymptomatic ID groups also reported higher self-perceived disease activity and increased axial pain, although peripheral joint pain was not a dominant feature, consistent with findings in patients with r-axSpA (27). Those with symptomat-

lesnika s axSpA-om (33). To je u skladu s hipotezom da se asimptomatski IK TMP klinički ne očituje kod bolesnika sa SpA-om, iako vjerojatno isti imunosno-patogenetski mehanizam postoji u osnovi bolesti, kao što se vidi kod bolesnika sa simptomatskim IK TMP-om, u kojem se bolest predočuje sa svim svojim glavnim simptomima (34). Disbioza crijeva i česta supklinička kronična upala crijeva temelj su različitih kliničkih predočavanja SpA-a (35), uključujući TMP (36). Sukladno tomu, povećana koncentracija α-amilaze u serumu mogla bi odražavati veću sposobnost umnažanja epitelnih stanica tankoga crijeva (37), što upućuje na izraženiju upalu kod bolesnika sa simptomatskim IK TMP-om nego u asimptomatskom i u kontrolnoj skupini. Tako osteoartritis (10, 38), a posebice pomak diska u TMZ-u (19), potkrijepljeni radiološkim nalazima, mogu biti potpuno asimptomatski, vjerojatno zbog nižeg stupnja upale i zahvaljujući velikim kompenzacijskim mehanizmima TMZ-a (19, 32).

MR je zlatni standard u dijagnostici IK TMP-a (12). U ovom istraživanju nije učinjen MR TMZ-a za bolesnika s asimptomatskim IK TMP-om, zato što se u sadašnjoj kliničkoj praksi često pretpostavlja da neznatni simptomi ne utječu znatno na bolesnika. Uz to, MR je skup i dugotrajan postupak koju obavljaju visoko educirani stručnjaci i uz to je ekonomski teret za zajednicu. Simptomatski IK TMP u ovom istraživanju dijagnosticiran je klinički s pomoću validiranog protokola Osi I za DK/TMP koji ima 97 % specifičnosti i 80 % osjetljivosti za otkrivanje bolnih TMP-ova (9, 5). Ovo je u skladu s odabirom bolesnika u nedavno objavljenoj metaanalizi koja se temelji na kliničkim i/ili radiografskim dokazima TMP-a (33). Visoka specifičnost i osjetljivost DK/TMP protokola olakšava dijagnosticiranje simptomatskoga IK TMP-a (11) i dijagnozu SpA-a u dobi od oko 30 godina, što je znatno ranije u usporedbi s bolesnicima sa zdravim TMZ-om. To je u skladu s tipičnom dobi za pojavu bolnoga aksijalnoga SpA-a (39), zato što bolovi, osobito oni kronični u TMZ-u, često potiču mlade odrasle osobe da potraže liječničku pomoć (7, 11, 15). Suprotno tomu, bolesnici s asimptomatskim IK TMP-om nisu osjetili bolove u TMZ-u, što vjerojatno objašnjava zašto se njihova dob početka SpA-a nije značajno razlikovala od one u kontrolnoj skupini. Stoga IK TMP može neko vrijeme napredovati asimptomatski, neprepoznat kao dio SpA-a pa se vjerojatno i neodgovarajuće liječi, iako se može vizualizirati MR-om (12). To može olakšati napredovanje IK TMP-a i pojavu r-axSpA-a. Doista, klinički parametri koji odražavaju aktivnost SpA-a, osobito biljezi aksijalne bolesti kao što je ASDAS-CRP (27), bili su povišeni kod asimptomatskih i simptomatskih bolesnika s IK TMP-om u usporedbi s kontrolom, što upućuje na podjednako opterećenje kad je riječ o zdravlju i kvaliteti života u objema skupinama bolesnika. Dobro je utvrđeno (23) i nedavno potvrđeno (40) da psorijatične promjene u bolnom TMZ-u pokazuju posljedice kronične upale (erozije) i izljev kao znak akutne upale oslikavanjem MR-om, što je u skladu s većom vrijednosti DAPSA-e kod bolesnika sa simptomatskim IK TMP-om u ovom istraživanju.

Bolesnici sa simptomatskim i asimptomatskim IK TMP-om također su prijavili veću samoprocijenjenu aktivnost bolesti i povećane aksijalne bolove, iako periferna bol u zglobo-

ic ID exhibited an elevated BASDAI alongside greater total body pain and enhanced difficulties performing all-day activities; however, these tools do not distinguish between axial and peripheral SpA activity (41).

Laboratory indicators further supported systemic inflammation in SpA patients with ID in relation to the controls. A reduction in hematocrit levels in both asymptomatic and symptomatic ID groups and a decrease in hemoglobin concentration in symptomatic ID foreshadow anemia of chronic disease, particularly in patients with symptomatic ID, which is predictive of functional impairment and axial SpA activity (42). Increased serum ASTO in both groups of patients with ID of TMD explains earlier streptococcal infection, which may have stimulated SpA activity, especially in carriers of the HLA-B27, B38, B39 and B8 genes (3).

The treatment of asymptomatic ID and their potential progression to symptomatic ID of TMJ in patients with SpA remains contentious. Progression may depend on the intensity and duration of the immune reaction in the TMJs, as observed in the progression of nr-axSpA to r-axSpA (4). In our patients, asymptomatic ID of TMJ was associated with more frequent exacerbation of r-axSpA, as resulted by ankylosis of the sacroiliac joints, found at the time of patients' recruitment, suggesting progressive axial disease. This connection between axial involvement and asymptomatic ID is supported by recent findings from de Melo-Silva et al. (33) and de Holanda et al. (8), as well as earlier studies linking occlusal interference and functional abnormalities of the cervical region and sacroiliac joints (43). Symptomatic TMDs have been associated with cervical spine pain (44) in patients with r-axSpA who tend to experience greater neck disability (32). Neck mobilization techniques have been shown to effectively improve maximal mouth opening and reduce pain in TMJs (45).

The data presented above showed the clinical implications of the research. Patients with symptomatic and asymptomatic IDs had statistically significantly increased patients' self-estimated axial pain and activity of SpA, as objectified with ASDAS and followed by the increased anti-streptolysin titre and decreased hematocrit than controls. Patients with symptomatic ID also had an earlier onset of SpA, along with increased disease activity indexes (BASDAI and DAPSA), total body pain, and difficulties in performing daily activities, increased platelet count, and serum alpha-amylase, but lower hemoglobin concentration than controls. Patients with asymptomatic ID had higher frequencies of exacerbated axial SpA and sacroiliac joint ankylosis compared to controls.

Conclusion

Both, asymptomatic and symptomatic IDs of TMJ in patients with SpA are associated with the activity of axial form of the disease, however the inflammatory process appears to

vima nije prevladavala, što je u skladu s nalazima bolesnika s r-axSpA-om (27). Bolesnici sa simptomatskim IK TMP-om imali su povišeni BASDAI te snažniju bol u cijelome tijelu i povećane poteškoće u obavljanju cjelodnevnih aktivnosti. No ti alati ne razlikuju aksijalnu i perifernu aktivnost SpA-e (41).

Laboratorijski pokazatelji dodatno su poduprli sustavnu upalu kod bolesnika sa SpA-om i IK TMP-om u usporedbi s kontrolnom skupinom. Smanjenje razine hematokrita u skupinama s asimptomatskim i simptomatskim IK TMP-om i smanjenje koncentracije hemoglobina u simptomatskom IK TMP-u nagovještavaju anemiju kronične bolesti, osobito kod bolesnika sa simptomatskim IK TMP-om, što je pokazatelj funkcijskog oštećenja i aksijalne aktivnosti SpA-a (42). Povećana serumska koncentracija ASTO-a u objema skupinama bolesnika s IK TMD-om objašnjava raniju infekciju streptokokom koja je mogla potaknuti aktivnost SpA-a, osobito kod nositelja gena *HLA-B27, B38, B39* i *B8* (3).

Liječenje asimptomatskoga IK TMP-a i njegovo moguće napredovanje do simptomatskoga IK TMP-a kod bolesnika sa SpA-om ostaje sporno. Napredovanje može ovisiti o jakosti i trajanju imunosne reakcije u TMZ-u, kao što je uočeno u napredovanju nr-axSpA-a u r-axSpA (4). Kod naših je bolesnika asimptomatski IK TMP bio povezan s češćom egzacerbacijom r-axSpA-e, što je rezultiralo ankilozom sakroilijačnih zglobova otkrivenom u vrijeme odabira bolesnika i upozorava na progresivnu aksijalnu bolest. Tu povezanost između aksijalnog zahvaćanja i asimptomatskoga IK TMP-a podupiru nedavni nalazi de Melo-Silve i suradnika (33) i de Holanda i suradnika (8) te prijašnje studije koje povezuju nepoželjne okluzijske dodire i funkcijske abnormalnosti vratne kralježnice i sakroilijačnih zglobova (43). Simptomatski TMP-ovi povezani su s bolovima u vratnoj kralježnici (44) kod bolesnika s r-axSpA-om koji imaju veće funkcijsko oštećenje vrata (32). Pokazalo se da tehnike mobilizacije vrata učinkovito poboljšavaju otvaranje usta u najvećoj mjeri i smanjuju bol u TMZ-u (45).

Gornji podatci upućuju na kliničke implikacije istraživanja. Bolesnici sa simptomatskim i asimptomatskim IK TMP-om izražavali su statistički značajno veću aksijalnu bol i aktivnost SpA-a prema samoprocjeni, što je objektivizirano ljestvicom ASDAS i praćeno povećanim titrom antistreptolizina i smanjenim hematokritom u odnosu prema kontroli. Bolesnici sa simptomatskim IK TMP-om dodatno su imali raniji početak SpA-a, zajedno s povećanim indeksima aktivnosti bolesti (BASDAI i DAPSA), bolovima u cijelom tijelu i poteškoćama u obavljanju svakodnevnih aktivnosti te povećanim brojem trombocita i serumskom koncentracijom α-amilaze, ali nižom koncentracijom hemoglobina od kontrole. Bolesnicima s asimptomatskim IK TMP-om češće se pojavljivalo pogoršanje aksijalnog SpA-a i ankiloza sakroilijačnoga zgloba u usporedbi s kontrolom.

Zaključak

Kod bolesnika sa SpA-om, asimptomatski i simptomatski IK TMP povezani su s aktivnošću aksijalnoga oblika bolesti, no čini se da je upalni proces izraženiji kod onih sa

be more pronounced in patients with symptomatic ID. Given the high prevalence of asymptomatic ID of TMJ in patients with SpA ongoing attention in clinical practice is needed to ensure early diagnosis of asymptomatic ID through radiologic imaging and timely treatment due to the significant burden on the health of these patients. The decision not to perform MRI on asymptomatic ID in this investigation is a limitation of this study and could have influenced patient group allocation. Another limitation could be the generalizability of the findings, since the study was conducted in a single hospital in Croatia, although the results are in line with previously published research conducted in other centers in Croatia and with those all over the world. Moreover, investigating immune mediators participating in the pathogenesis of SpA, with clinically relevant diagnostic value for asymptomatic ID, can be of particular interest for simple, economically acceptable, and timely diagnosis.

Acknowledgement: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding: This research was financed by the University of Rijeka, Croatia (Grant No.- Uni-ri-biomed-18-160) from March 7, 2019 to May 31, 2023.

Author's contribution: A.M.L. - investigation (conducting a clinical investigation and data/evidence collection), data curation and analyses, writing - original draft of manuscript, including substantive translation; **S.Š.** - validation (verification of clinical examination of temporomandibular joints); **G. L.**- validation of rheumatological data, formal analysis (application of statistical techniques and synthesize study data), visualization; **A.R.B.** - investigation (performing the radiological methods); **J.G.** -: validation (verification of laboratory analyses, reproducibility of results); **E.B. -** formal analysis (application of statistical techniques to analyze study data); **T.K.** -project administration (coordination responsibility for the research activity planning and execution), funding acquisition (project leading); **V.P.** - funding acquisition; **N.D.** - conceptualization, supervision (oversight and leadership responsibility for the research activity planning and execution, including mentorship), writing (review and editing).

simptomatskim IK TMP-om. S obzirom na visoku prevalenciju asimptomatskoga IK TMP-a kod bolesnika sa SpA-om, potrebna je stalna pozornost u kliničkoj praksi kako bi se osigurala rana dijagnoza asimptomatskoga IK TMP-a putem radiološkog oslikavanja i pravodobnog liječenja, zbog značajnog opterećenja zdravlja tih bolesnika. Odluka da se u ovom istraživanju ne upute na MR bolesnici s asimptomatskim IK TMP-om ograničenje je ove studije i moglo bi utjecati na raspodjelu bolesnika u skupine. Drugo ograničenje mogla bi biti generaliziranost nalaza zato što je istraživanje provedeno u jednoj bolnici u Hrvatskoj, iako su rezultati u skladu s već objavljenim istraživanjima provedenima u drugim centrima u Hrvatskoj i diljem svijeta. Istraživanje imunosnih posrednika koji sudjeluju u patogenezi SpA-a, s kliničkom dijagnostičkom vrijednošću za asimptomatski IK TMP, bilo bi posebno zanimljivo zbog pravodobnog postavljanja dijagnoze na jednostavan i ekonomski prihvatljiv način.

Priznanje: Autori izjavljuju da nemaju poznatih suprotstavljenih financijskih interesa ili osobnih odnosa koji bi mogli utjecati na rad o kojemu se izvješćuje u ovom članku.

Financiranje: Ovo istraživanje financiralo je Sveučilište u Rijeci, Hrvatska (potpora br. Uni-ri-biomed-18-160) od 7. ožujka 2019. do 31. svibnja 2023.

Doprinos autora: A. M. L. – istraživanje (kliničko istraživanje i prikupljanje podataka/dokaza), čuvanje podataka i analize, pisanje - izvorni nacrt rukopisa, uključujući suštinsku preobrazbu; **S. Š.** – validacija (verifikacija kliničkog pregleda temporomandibularnih zglobova); **G. L.** – validacija reumatoloških podataka, formalna analiza (primjena statističkih tehnika i sinteza podataka istraživanja), vizualizacija; **A. R. B.** – istraživanje (provođenje radioloških metoda); **J. G.** – validacija (verifikacija laboratorijskih analiza, ponovljivost rezultata); **E. B.** – formalna analiza (primjena statističkih tehnika za analizu podataka istraživanja); **T. K.** – upravljanje projektom (odgovornost za koordinaciju planiranja i provedbe istraživačkih aktivnosti), nabava financijskih sredstava (vođenje projekta); **V. P.** – nabava financijskih sredstava; **N. D.** – konceptualizacija, nadzor (odgovornost za nadgledanje i vođenje planiranja i provedbe istraživačkih aktivnosti, uključujući mentorstvo), pisanje (recenzija i uređivanje)

Sažetak

Cilj rada: Skupina bolesti spondiloartritisa (SpA) ima zajedničke kliničke pojavnosti, uključujući intrakapsularni temporomandibularni poremećaj (IK TMP). Ovo istraživanje imalo je za cilj istražiti aktivnost SpA-e kod bolesnika s IK TMP-om. **Materijali i metode:** Dijagnosticirali smo SpA kod 200 bolesnika s bolovima u vratu koristeći se međunarodnom razradbom ASAS (engl. The Assessment of SpondyloArthritis International Society). Temporomandibularni zglob (TMZ) pregledan je s pomoću protokola Dijagnostički kriteriji za temporomandibularne poremećaje (DK/TMP). Bolesnici sa SpA-om podijeljeni su u tri skupine: simptomatski IK TMP, asimptomatski IK TMP ili zdravi TMZ (kontrola). Aktivnost SpA-e procijenjena je korištenjem ASDAS-a (engl. Ankylosing Spondylitis Disease Activity Score), BASDAI-ija (engl. Bath Ankylosing Spondylitis Disease Activity Index), DAPSA-e (engl. Disease Activity Index in Psoriatic Arthritis), aktivnosti SpA-e koju su bolesnici sami procijenili, poteškoća u obavljanju dnevnih aktivnosti, jakosti bolova (vizualna analogna ljestvica) i laboratorijskim parametrima. **Rezultati:** Bolesnici sa simptomatskim i asimptomatskim IK TMP-om imali su statistički značajno veći ASDAS, titar antistreptolizina, samoprocjenu aksijalne boli i aktivnost SpA-e te smanjeni hematokrit u odnosu prema kontroli. Bolesnici sa simptomatskim IKTMP-om dodatno su imali statistički značajno raniji početak SpA-e, zajedno s povećanim BASDAI-jem i DAPSA-om, bolovima u cijelom tijelu, poteškoćama u obavljanju dnevnih aktivnosti, broju trombocita i koncentracijom α-amilaze u serumu, ali manju koncentraciju hemoglobina od kontrole. Bolesnici s asimptomatskim IK TMP-om imali su veću učestalost pogoršanja aksijalnoga spondiloartritisa (SpA) i ankiloze sakroilijačnoga zgloba u usporedbi s kontrolom. **Zaključak:** Kod svih bolesnila sa SpA-om i IK TMP-om zabilježena je povećana aksijalna aktivnost bolesti.

Zaprimljen: 17. listopada 2024.
Prihvaćen: 2. ožujka 2025.

Adresa za dopisivanje
Ana-Marija Laškarin, dr. med., doktorandica
Sveučilište u Zagrebu
Stomatološki fakultet
Gundulićeva 5, HR-10000 Zagreb
tel: +385 91 790 5139
alaskarin@sfzg.hr

MeSH pojmovi: poremećaji čeljusnog zgloba; aksijalni spondiloartritis
Autorske ključne riječi: spondiloartritis, temporomandibularni poremećaji, unutarnji poremećaji temporomandibularnog zgloba

References

1. Taams LS, Steel KJA, Srenathan U, Burns LA, Kirkham BW. IL-17 in the immunopathogenesis of spondyloarthritis. Nat Rev Rheumatol. 2018 Aug;14(8):453-466.
2. Walsh JA, Magrey M. Clinical manifestations and diagnosis of axial spondyloarthritis. J Clin Rheumatol. 2021 Aug;27(8):e547-e560.
3. FitzGerald O, Haroon M, Giles JT, Winchester R. Concepts of pathogenesis in psoriatic arthritis: genotype determines clinical phenotype. Arthritis Res Ther. 2015 Apr;17(1):115.
4. Robinson PC, van der Linden S, Khan MA, Taylor WJ. Axial spondyloarthritis: concept, construct, classification and implications for therapy. Nat Rev Rheumatol. 2021 Feb;17(2):109-118.

5. Souza RC, de Sousa ET, Sousa D, Sales M, Dos Santos Oliveira R, Mariano MH, et al. Prevalence of temporomandibular joint disorders in patients with ankylosing spondylitis: A cross-sectional study. Clin Cosmet Investig Dent. 2021;13:469-478.
6. Dinneen B, O'Shea F, Gensler L. Structural disease modification in axial spondyloarthritis. Best Pract Res Clin Rheumatol. 2023 Sep;37(3):101898.
7. Kazeminasab S, Nejadghaderi SA, Amiri P, Pourfathi H, Araj-Khodaei M, Sullman MJM, et al. Neck pain: global epidemiology, trends and risk factors. BMC Musculoskelet Disord. 2022 Jan;23(1):26.
8. de Holanda GA, de Holanda TA, Boscato N, Casarin M. Temporomandibular joint involvement in individuals with ankylosing spondylitis: A scoping review. Arch Oral Biol. 2023 Jan;146:105609.
9. Schiffman E, Ohrbach R, Truelove E, Look J, Anderson G, Goulet JP, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for clinical and research applications: recommendations of the International RDC/TMD Consortium Network and Orofacial Pain Special Interest Group. J Oral Facial Pain Headache. 2014 Jan;28(1):6-27.
10. Vrbanović E, Alajbeg IZ. A Young Patient with Temporomandibular Joint Osteoarthritis: Case Report. Acta Stomatol Croat. 2017 Sep;51(3):232-239.
11. Vrbanović E, Dešković K, Zlendić M, Alajbeg IZ. Profiling of patients with temporomandibular disorders: experience of one tertiary care center. Acta Stomatol Croat. 2021 Jun;55(2):147-158.
12. Badel T, Vojnović S, Buković D, Zadravec D, Anić Milošević S, Smoljan Basuga M, et al. The asymmetry of the mandible in patients with unilateral temporomandibular joint disc displacement confirmed by magnetic resonance imaging. Acta Stomatol Croat. 2023 Jun;57(2):167-176.
13. Tanaka E, Detamore MS, Mercuri LG. Degenerative disorders of the temporomandibular joint: etiology, diagnosis, and treatment. J Dent Res. 2008 Apr;87(4):296-307.
14. Alajbeg IZ, Vrbanović E, Lapić I, Alajbeg I, Vuletić L. Effect of occlusal splint on oxidative stress markers and psychological aspects of chronic temporomandibular pain: a randomized controlled trial. Sci Rep. 2020 Jul;10(1):10981.
15. Beaumont S, Garg K, Gokhale A, Heaphy N. Temporomandibular disorder: a practical guide for dental practitioners in diagnosis and management. Aust Dent J. 2020 Sep;65(3):172-180.
16. Lee YH, Auh QS. Comparison of sleep quality deterioration by subgroup of painful temporomandibular disorder based on diagnostic criteria for temporomandibular disorders. Sci Rep. 2022 Jun;12(1):9026.
17. Ibi M. Inflammation and temporomandibular joint derangement. Biol Pharm Bull. 2019 Apr;42(4):538-542.
18. Wolford LM. Understanding TMJ reactive arthritis. Cranio. 2017 Sep;35(5):274-275.
19. Molinari F, Manicone PF, Raffaelli L, Raffaelli R, Pirronti T, Bonomo L. Temporomandibular joint soft-tissue pathology, I: disc abnormalities. Semin Ultrasound CT MR. 2007 Jun;28(3):192-204.
20. García-Kutzbach A, Chacón-Súchite J, García-Ferrer H, Iraheta I. Reactive arthritis: update 2018. Clin Rheumatol. 2018 Apr;37(4):869-874.
21. So J, Tam LS. Gut microbiome and its interaction with immune system in spondyloarthritis. Microorganisms. 2020 Nov;8(11):1727.
22. Vitale A, Caggiano V, Silva I, Oliveira DG, Ruscitti P, Ciccia F, et al. Axial spondyloarthritis in patients with recurrent fever attacks: data from the AIDA network registry for undifferentiated autoinflammatory diseases (USAIDs). Front Med (Lausanne). 2023 Jul;10:1195995.
23. Badel T, Savić Pavičin I, Krapac L, Zadravec D, Rosić D. Psoriatic arthritis and temporomandibular joint involvement - literature review with a reported case. Acta Dermatovenerol Croat. 2014 Jun;22:114-121.
24. Crincoli V, Di Comite M, Di Bisceglie MB, Fatone L, Favia G. Temporomandibular disorders in psoriasis patients with and without psoriatic arthritis: an observational study. Int J Med Sci. 2015 Apr;12(4):341-348.
25. Shim JS, Kim C, Ryu JJ, Choi SJ. Correlation between TM joint disease and rheumatic diseases detected on bone scintigraphy and clinical factors. Sci Rep. 2020 Mar;10(1):4547.
26. Rudwaleit M, van der Heijde D, Landewé R, Akkoc N, Brandt J, Chou CT, et al. The Assessment of Spondyloarthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis. 2011 Jan;70(1):25-31.
27. Proft F, Muche B, Spiller L, Rios Rodriguez V, Rademacher J, Weber AK, et al. Performance of the ankylosing spondylitis disease activity score based on a quick quantitative C-reactive protein assay in patients with axial spondyloarthritis. Joint Bone Spine. 2020 Jan;87(1):69-73.
28. Grazio S, Grubisić F, Nemcić T, Matijević V, Skala H. The reliability and validity of a Croatian version of the Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) in patients with ankylosing spondylitis. Reumatizam. 2009 Jun;56(2):63-76.
29. Gonçalves RSG, de Almeida Martins LM, de Ataide Mariz H, Dantas AT, Duarte ALBP. DAPSA versus cDAPSA: Do we need to use CRP? Ann Rheum Dis. 2020 Nov;79(11):e142.
30. Ohrbach R, Knibbe W. [Internet]. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD). Scoring Manual for Self-Report Instruments. University at Buffalo, NY, US and ACTA, Amsterdam, The Netherlands, Version: January 9, 2017. [updated 2017 Jan 9; cited 2020 Oct 18]. Available from:https://ubwp.buffalo.edu/rdc-tmdinternational/wp content/uploads/sites/58/2017/01/DC-TMD-Self-report-Instrument-Scoring-Manual_2017_01_09.pdf
31. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD): Diagnostic Decision Tree, (2013). [Internet], <available at: https://pdfcoffee.com/dc-tmd-decision-trees20130608-pdf-free.html>, [cited 2021 Jan 31].
32. Syrmou V, Grammatikopoulou MG, Bogdanos DP, Mitsimponas KT. Temporomandibular joint disorders in seronegative spondyloarthritis: what a rheumatologist needs to know? Reumatologia. 2023 Oct;61(5):375-388.
33. de Melo-Silva EMV, Valdez RA, da Barbosa-Silva IM, Chateaubriand MM, Duarte ALBP, Gueiros LA. Association between axial spondyloarthritis and temporomandibular disorders: A systematic review. Oral Dis. 2023 Jul;29(7):2592-2599.
34. Laskarin AM, Laskarin G, Kehler T, Grzic R, Dulcic N. Assessment of internal derangement of the temporomandibular joint according to the concentration of salivary cytokines in patients with spondyloarthritis. Med Hypotheses. 2023 Jan;170:111000.
35. Tsukazaki H, Kaito T. The role of the IL-23/IL-17 pathway in the pathogenesis of spondyloarthritis. Int J Mol Sci. 2020 Sep;21(17):6401.
36. Zhao K, Ji S, Jiang H, Qian Y, Zhang W. Exploring the gut microbiota's effect on temporomandibular joint disorder: a two-sample Mendelian randomization analysis. Front Cell Infect Microbiol. 2024 Feb;14:1361373.
37. Date K, Yamazaki T, Toyoda Y, Hoshi K, Ogawa H. α-Amylase expressed in human small intestinal epithelial cells is essential for cell proliferation and differentiation. J Cell Biochem. 2020 Feb;121(2):1238-1249.
38. Derwich M, Mitus-Kenig M, Pawlowska E. Interdisciplinary approach to the temporomandibular joint osteoarthritis—review of the literature. Medicina (Kaunas). 2020 May;56(5):225.
39. Arevalo Salaet M, López-Medina C, Moreno M, Navarro-Compan V, Calvet Fontova J, Llop M, et al. Association between HLA-B27 and peripheral spondyloarthritis phenotype: results from the ASAS perSpA study. RMD Open. 2022 Aug;8(2):e002696.
40. Almășan O, Hedeșiu M, Băciuț M, Buduru S, Dinu C. Psoriatic arthritis of the temporomandibular joint: A systematic review. J Oral Rehabil. 2023 Mar;50(3):243-255.
41. Reddy SM, Xue K, Husni ME, Scher JU, Stephens-Shields AJ, Goel N, et al. Use of the Bath Ankylosing Spondylitis Disease Activity Index in patients with psoriatic arthritis with and without axial disease. J Rheumatol. 2024 Feb;51(2):139-143. doi: 10.3899/jrheum.2023-0504.
42. Li H, Li Q, Duan X, Zhang S, Wang Y, Xu J, et al. Anemia and low body mass index in axial spondyloarthritis: results from ChinaSpA, the Chinese Spondyloarthritis Registry. Rheumatol Ther. 2024 Feb;11(2):397-409.
43. Fink M, Wähling K, Stiesch-Scholz M, Tschernitschek H. The functional relationship between the craniomandibular system, cervical spine, and the sacroiliac joint: a preliminary investigation. Cranio. 2003 Jul;21(3):202-8.
44. La Touche R, Martínez García S, Serrano García B, Proy Acosta A, Adraos Juárez D, Fernández Pérez JJ, et al. Effect of manual therapy and therapeutic exercise applied to the cervical region on pain and pressure pain sensitivity in patients with temporomandibular disorders: A systematic review and meta-analysis. Pain Med. 2020 Oct;21(10):2373-2384.
45. Calixtre LB, Moreira RF, Franchini GH, Alburquerque-Sendín F, Oliveira AB. Manual therapy for the management of pain and limited range of motion in subjects with signs and symptoms of temporomandibular disorder: a systematic review of randomised controlled trials. J Oral Rehabil. 2015 Nov;42(11):847-61.