

Citation: Jha N, Lee K-s, Kim Y-J (2022) Diagnosis of temporomandibular disorders using artificial intelligence technologies: A systematic review and meta-analysis. PLoS ONE 17(8): e0272715. https://doi.org/10.1371/journal.pone.0272715

Editor: Essam Al-Moraissi, Thamar University, Faculty of Dentistry, YEMEN

Received: January 20, 2022

Accepted: July 25, 2022

Published: August 18, 2022

Copyright: © 2022 Jha et al. This is an open access article distributed under the terms of the <u>Creative</u> Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the paper and its <u>Supporting Information</u> files.

Funding: YES-The National Research Foundation of Korea funded by the Ministry of Science and ICT of South Korea (grant 2019R1C1C1009881 and 2022R1H1A2011172) supported in the collection, analysis, and interpretation of data and in writing the manuscript.

Competing interests: The authors have declared that no competing interests exist.

RESEARCH ARTICLE

Diagnosis of temporomandibular disorders using artificial intelligence technologies: A systematic review and meta-analysis

Nayansi Jha¹, Kwang-sig Lee², Yoon-Ji Kim³*

1 University of Ulsan College of Medicine, Seoul, Korea, 2 Al Center, Korea University Anam Hospital, Korea University College of Medicine, Seoul, Korea, 3 Department of Orthodontics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

* yn0331@ulsan.ac.kr

Abstract

Background

Artificial intelligence (AI) algorithms have been applied to diagnose temporomandibular disorders (TMDs). However, studies have used different patient selection criteria, disease subtypes, input data, and outcome measures. Resultantly, the performance of the AI models varies.

Objective

This study aimed to systematically summarize the current literature on the application of AI technologies for diagnosis of different TMD subtypes, evaluate the quality of these studies, and assess the diagnostic accuracy of existing AI models.

Materials and methods

The study protocol was carried out based on the preferred reporting items for systematic review and meta-analysis protocols (PRISMA). The PubMed, Embase, and Web of Science databases were searched to find relevant articles from database inception to June 2022. Studies that used AI algorithms to diagnose at least one subtype of TMD and those that assessed the performance of AI algorithms were included. We excluded studies on orofacial pain that were not directly related to the TMD, such as studies on atypical facial pain and neuropathic pain, editorials, book chapters, and excerpts without detailed empirical data. The risk of bias was assessed using the QUADAS-2 tool. We used Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) to provide certainty of evidence.

Results

A total of 17 articles for automated diagnosis of masticatory muscle disorders, TMJ osteoarthrosis, internal derangement, and disc perforation were included; they were retrospective studies, case-control studies, cohort studies, and a pilot study. Seven studies were subjected to a meta-analysis for diagnostic accuracy. According to the GRADE, the certainty of evidence was very low. The performance of the AI models had accuracy and specificity ranging from 84% to 99.9% and 73% to 100%, respectively. The pooled accuracy was 0.91 (95% CI 0.76–0.99), $I^2 = 97\%$ (95% CI 0.96–0.98), p < 0.001.

Conclusions

Various AI algorithms developed for diagnosing TMDs may provide additional clinical expertise to increase diagnostic accuracy. However, it should be noted that a high risk of bias was present in the included studies. Also, certainty of evidence was very low. Future research of higher quality is strongly recommended.

Introduction

Temporomandibular disorders (TMDs) can cause pain and dysfunction in the temporomandibular joints (TMJs) and masticatory muscles. TMDs are the second most common musculoskeletal conditions and include various symptoms, such as decreased range of motion, joint sound, and mouth opening deviation [1]. TMDs can be classified as pain-related disorders, which include myalgia and arthralgia, and intra-articular disorders, which include internal derangement and degenerative joint disease (DJD) [2].

The etiology of TMDs is considered multifactorial, with biological, behavioral, and psychosocial factors contributing independently or as interrelated factors [3, 4]. Moreover, comorbidities, such as cardiovascular diseases, osteoarthritis, tinnitus, sinusitis, and thyroid disorders, are associated with disease onset and progression [5–7]. Therefore, diagnosis of TMDs requires a comprehensive evaluation of the patients' signs and symptoms (acquired through clinical examination and medical image analysis) and behavioral and psychosocial factors [2, 8]. Subsequently, the complex nature of TMDs makes diagnosis difficult.

Currently, the most widely accepted diagnostic criteria is the Diagnostic Criteria for Temporomandibular Disorders (DC-TMD) [2] which was developed on the basis of largescale international studies and data analyses since the 1990s. The DC-TMD comprises two axes, Axis I and Axis II, which include diagnostic standards for differentiating pain-related TMDs and intra-articular disorders (Axis I) and assessing jaw function and behavioral and psychosocial factors (Axis II).

Despite the popularity of the DC-TMD, it has limitations in terms of its diagnostic accuracy. Several subtypes of internal derangement, such as disc displacement with reduction, with reduction and locking, and without reduction, showed low sensitivity (0.34–0.54). Similarly, low sensitivity (0.55) and specificity (0.61) were observed for DJD. Further, the interexaminer reliability is relatively low for internal derangement and DJD [2]. Screening tools, such as surveys to determine patients' symptoms, are expensive and time-consuming and place a burden on clinicians.

Advancements in artificial intelligence (AI) technologies have led to major developments in the healthcare industry. The Merriam–Webster dictionary defines AI as 'the capability of a machine to imitate intelligent human behavior.' It essentially refers to the simulation of human intelligence processes using computer systems. Generally, AI systems are trained using large amounts of input data. Patterns are learned from these data and then used to predict the outcome of new instances. AI algorithms are increasingly applied in patient diagnoses, especially for detecting and classifying lesions, such as skin cancers [9], diabetic retinopathy [10], brain tumors [11], and dental caries [12], using medical diagnostic images [13]. Additionally, other data types, such as electronic medical records in the form of text [14], voice [15], and sound [16] are used to develop diagnostic tools to support clinicians in decision-making.

Recently, various AI algorithms have been applied to image and nonimage data for TMDs diagnosis [17–21]. However, studies on the use of AI for TMD diagnosis have used different patient selection criteria, disease subtypes, input data used for diagnosis, and outcome measures for performance evaluation. Moreover, the accuracy of the AI models varies. To the best of our knowledge, there has been no systematic review till date that summarizes such findings. Therefore, this study aimed to systematically summarize the current literature on the application of AI technologies for diagnosis of different TMD subtypes—both muscular and articular conditions—evaluate the quality of these studies and assess the diagnostic accuracy of existing AI models.

Materials and methods

This systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) 2020 guide-lines (S1 and S2 Tables) [22].

Research questions

This systematic review and meta-analysis was conducted to answer the following question: "How accurate are the AI algorithms for the diagnosis of TMDs?" The focused question was further classified as follows:

- 1. Which data were used for developing algorithms for TMD diagnosis?
- 2. Which AI techniques were used for TMD diagnosis?
- 3. Which features were used for TMD diagnosis?
- 4. Which outcome measures were used for assessing the model performance?

Further, the research question was formatted using the Population, Intervention, Comparison, and Outcome framework (Table 1).

Information sources and search strategy

Our search algorithm comprised the PubMed, EMBASE, and Web of Science databases. A combination of the following terms was used: "artificial intelligence" OR "neural network" OR "machine learning" OR "deep learning" OR/AND "TMJ osteoarthritis" OR "temporomandibular joint osteoarthritis" OR "temporomandibular disorders" OR "masticatory muscle disorders" OR "TMDs" OR "TMJ disorder" OR "temporomandibular joint disorders" OR "TMJ

Table 1. Description of the population, intervention, comparison, and outcome elements.

Research question	How accurate are the AI algorithms for the diagnosis of TMDs?
Population	Patients with TMDs
Intervention	Use of medical diagnostic images (CBCT, MRI, panoramic radiographs) and health records
Comparison	Type of data and algorithm used for AI-based automated diagnosis models
Outcome	Performance of AI algorithms for the diagnosis of TMDs assessed using diagnostic accuracy

AI, artificial intelligence; TMDs, temporomandibular disorders; CBCT, cone-beam computed tomography; MRI, magnetic resonance imaging

https://doi.org/10.1371/journal.pone.0272715.t001

arthritis" OR "temporomandibular joint arthritis" OR "progressive condylar resorption" OR "degenerative joint disease" OR "temporomandibular joint disease" OR "TMJ disease" OR "idiopathic condylar resorption" OR "juvenile idiopathic arthritis." No start date was used, whereas the end date was June 30, 2022. <u>Table 2</u> includes the search strategy for each database.

Eligibility criteria, study selection, and data collection

We included original studies published in scientific journals whose full texts were available. The inclusion criteria were as follows: (a) use of AI algorithms to diagnose at least one subtype of TMDs; (b) the performance of the developed AI algorithms was assessed; (c) no limit on the participants in terms of gender, age, or ethnicity; and (d) were written in English. The exclusion criteria were as follows: (a) studies on orofacial pain that is not directly related to the TMJ, such as atypical facial pain and neuropathic pain; (b) studies on TMJ that were unrelated to disease diagnosis; (c) editorials, comments, book chapters, and excerpts without detailed empirical data; and (d) studies not written in English.

To determine the final eligibility, the two investigators (YJK and NJ) independently assessed the full text of studies. Conflicts between the reviewers was resolved by the involvement of a third investigator (KSL). Then, two investigators, NJ and YJK, independently extracted and formulated the data, such as input data used for TMD diagnosis, AI algorithms used, and performance measures. Any discrepancies were resolved through discussion.

Risk of bias assessment

The selected articles were critically assessed and scored independently by two investigators (YJK and NJ). Quality assessment of the studies was based on the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) [23]. The QUADAS tool was first developed in 2003 for systematic reviews of diagnostic accuracy studies and later updated to QUADAS-2. It

Database	Search Terms	Records retrieved
PubMed	("artificial intelligence " OR " neural network " OR " machine learning " OR " deep learning ")) AND/OR (("TMJ osteoarthritis" OR "Temporomandibular joint osteoarthritis" OR " Temporomandibular disorders " OR "TMDs" OR "TMJ disorder" OR "Temporomandibular joint disorders" OR "TMJ arthritis" OR "Temporomandibular joint arthritis" OR "masticatory muscle disorder" OR "progressive condylar resorption" OR "degenerative joint disease" OR "Temporomandibular joint disease" OR "TMJ disease" OR	1142
Embase	("artificial intelligence " OR " neural network " OR " machine learning " OR " deep learning ")) AND/OR ((" TMJ osteoarthritis " OR " Temporomandibular joint osteoarthritis" OR " Temporomandibular disorders " OR " TMDs" OR " TMJ disorder" OR " Temporomandibular joint disorders" OR " TMJ arthritis" OR " Temporomandibular joint arthritis" OR "masticatory muscle disorder" OR "progressive condylar resorption" OR " degenerative joint disease" OR " Temporomandibular joint disease" OR " TMJ disease" OR " Temporomandibular joint disease" OR " TMJ disease" OR "	585
Web of Science	("artificial intelligence " OR " neural network " OR " machine learning " OR " deep learning ")) AND/OR ((" TMJ osteoarthritis " OR " Temporomandibular joint osteoarthritis" OR " Temporomandibular disorders " OR " TMDs" OR " TMJ disorder" OR " Temporomandibular joint disorders" OR " TMJ arthritis" OR " Temporomandibular joint arthritis" OR "masticatory muscle disorder" OR " progressive condylar resorption" OR " degenerative joint disease" OR " Temporomandibular joint disease" OR " TMJ disease" OR " resorption" OR " juvenile idiopathic arthritis")	196

Table 2. Search strategy for each database.

https://doi.org/10.1371/journal.pone.0272715.t002

comprises four components: patient selection, index test, reference standard, and flow and timing. Each component is assessed for the risk of bias. The first three components are also assessed for concerns about the applicability of each component [23]. The quality was rated as high, low, or unclear. Conflicts between the reviewers was resolved by the involvement of a third investigator (KSL).

Certainty of evidence assessment

We used Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) [24] to evaluate the quality of evidence of studies for which meta-analysis was performed. Each outcome gets a rating on the quality of evidence of high, moderate, low, or very low within five domains- risk of bias, imprecision, inconsistency, indirectness, and publication bias.

Statistical analysis

Meta-analysis of diagnostic accuracy was conducted using the Hartung–Knapp–Sidik–Jonkman method for random-effects models. The accuracy estimates were transformed using the Freeman–Tukey double arcsine method. Heterogeneity was quantified using the I^2 statistic, which is the percentage of total variation across studies due to heterogeneity rather than chance. All analyses were conducted using R v.4.0.4 (R Project for Statistical Computing) with the Meta package.

Results

Study selection

The initial database search yielded 1923 studies. After removing duplicate studies, 985 articles were screened for inclusion, of which 32 studies corresponded to TMD diagnosis using AI. However, 15 of these 32 articles were excluded due to various reasons, such as book chapters, studies with a focus on creating a web system repository for neural data storage, studies related to TMJ movement and anatomy, excluding diagnosis, studies related to facial pain syndrome as a differential diagnosis, and studies related to robotics (S3 Table). Finally, 17 articles met our eligibility criteria and were included in this systematic review (Fig 1).

Risk of bias assessment of the included studies

Fig 2 summarizes the study biases as high, low, or unclear. The patient selection bias potential was low in 11 out of 17 studies [17, 19, 21, 25–32] and high in 6 out of 17 studies [18, 20, 33–36]. A high risk of bias in patient selection was present due to the inclusion of case-control studies. However, the applicability concerns for patient selection were assessed as low for these studies because selection bias was overcome using case-control matching. Regarding the reference test and flow and timing domains, 17 out of 17 studies were considered to have a low degree of bias and low degree of applicability (S1 Fig). Index test was reported unclear for 13 out of 17 studies due to a lack of information on threshold values.

Certainty of evidence assessment of the included studies

Of the 7 studies considered for meta-analysis, 2 studies had invalid outcomes for the test of diagnostic accuracy. Therefore, 5 studies were included for the GRADE analysis [17, 18, 28, 33, 34]. According to the GRADE, the Risk of bias was considered serious as it was high for three studies [18, 33, 34]. The factor of imprecision was considered very serious because the number of subjects was less than 1000 [17, 18, 33, 34]. Therefore, the certainty of evidence was concluded as very low (S4 Table).

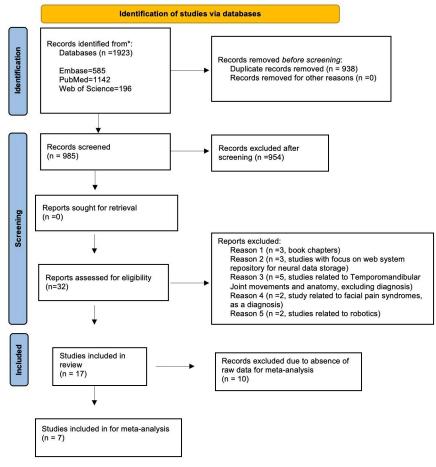
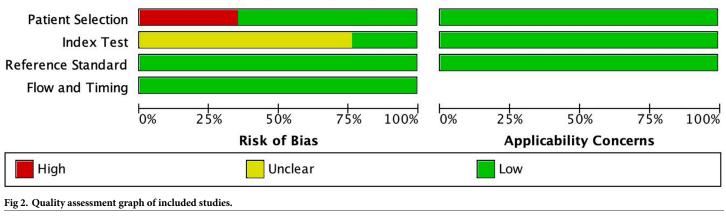


Fig 1. PRISMA flowchart for screening and identifying the included studies.

https://doi.org/10.1371/journal.pone.0272715.g001

Characteristics of the included studies

The types of studies included were mostly retrospective studies [17, 20, 21, 25, 26, 28, 30–33], 3 case-control studies [18, 19, 29, 34], 2 case-control cohort studies [35, 36], and 1 pilot study [27]. Table 3 shows the characteristics of the included studies.



https://doi.org/10.1371/journal.pone.0272715.g002

Control District of the second second second biology District of the second second second biology District of the second second second biology District of the second second biology - <t< th=""><th>Table 3. Charae</th><th>Table 3. Characteristics of the included studies. Author Vear Samula</th><th>ncluded studies. Study objective</th><th>Tyme of</th><th>Alcorithme</th><th>TMD subtrue</th><th>Critoria for</th><th>Datacat ciza</th><th>Reatures used</th><th>Daenite (Darformanca</th></t<>	Table 3. Charae	Table 3. Characteristics of the included studies. Author Vear Samula	ncluded studies. Study objective	Tyme of	Alcorithme	TMD subtrue	Critoria for	Datacat ciza	Reatures used	Daenite (Darformanca
 Artificial reuri revolk for revolk for revolk	Ical	description (age in years and/ or sex)		rype or Data used	used	studied*	diagnosing TMD subtype	Dataset size	for training	Acsuls/Feriorinance
-Automatic facial terveen individuals vith rMD and individuals vith rMD and restriction riddials vith rMD and rMD	al.,		Artificial neural network for detection of normal TMJs and non- reducing displaced disks	Medical records	ANN	Internal derangement	medical history, clinical examination findings, joint vibration analysis findings, electromyographic findings, and using tomographic x-rays	Training set: 34 Testing set: 34	Incisal chewing patterns	a) Specificity: 100% b) Sensitivity: 91.8% c) Accuracy: 86.8%
-Use of ANN for diagnosis of TMJ ID and Dormal jointsMedical herangement ceroting to RDC/ Testing set S8Mering set: conting stand jaw according to RDC/ Testing set S8Clicking joint sounds, and jaw1TAge:BN application according to RDC/Iraining set: conding to RDC/Clicking joint according to RDC/Clicking joint according to RDC/1Age:BN applicationMRIANN; according to RDC/Iraining set: according to RDC/Clicking set S81Age:BN applicationMRIANN; actionInternal derangement actionClicking set S8Clicking set S81Age:DNANN; actionInternal derangement actionNO-Disc1Age:DNANN; author (bony, author (bony, author (bony, danges and disc-DiscDisc2.Sex: 54DNDSex: 54Sex: 54Sex: 54Sex: 54Pathon author (bony, changes and disc-Disc2.Sex: 54DNDSex: 54Sex: 54Sex: 54Sex: 54Sex: 54Sex: 5411DNDDathon author (bony, chreelyDiscDisc2.11Early PolyChreelyDiscClicking Set	Ghodsi et al.,2007 [19]		Automatic facial pattern classification between individuals with TMD and healthy individuals	High- resolution video camera	MVS	TMD (no subtype)	clinical examination findings	Mandible movements		Lyapunov exponent (λ ₁) larger for individuals with TMD than those for healthy subjects
1. Age:BBN applicationMRIANN;InternalRDC/TMD or-Disca) Ageto MRI forBayesianderangementdefined by thepointdisplacementRange:11-86diagnosis ofpathderangementdefined by theand bonyD) AverageTMDsand TMJOAauthor (bonychanges and discb) AverageTMDscondition,changes and discchanges withinage:39:5Condition,Greedyauthor (bonychanges and disc2.Sex: 54sextch-and-sextch-and-displacement)TMJanales,sextch-and-sextch-and-sextch-and-changes within241 femaleschanges and discchanges and discchanges within241 femalesexotch-and-sextch-and-sextch-and-261 femalesexotch-and-bychanges and disc271 femalesexotch-and-sextch-and-281 femalesexotch-and-exotch-and-291	[25]		Use of ANN for diagnosis of TMJ ID and normal joints	Medical records	ANN	Internal derangement	Patient histories and clinical symptoms, according to RDC/ TMD*	Training set: 161 Testing set: 58	Clicking, joint sounds, and jaw deviation	Unilateral ADDwR a) Sensitivity: 80% b) Specificity: 95% Unilateral ADDwoR a) Sensitivity: 69% b) Specificity: 91% Bilateral ADDwR a) Sensitivity: 100% b) Specificity: 89% One side ADDwR, other side ADDwoR a) Sensitivity: 44% b) Specificity: 93%
	[21]	1. Age: a) Age Range:11-86 b) Average age:39.5 2. Sex : 54 males, 241 females	BBN application to MRI for diagnosis of TMDs	MRI	ANN; Bayesian belief network path condition, Greedy search-and- score, Bayesian information criterion, Chow-Liu tree, Rebane- Pearl poly tree, Naïve Bayes	Internal derangement and TMJOA	RDC/TMD or defined by the author (bony changes and disc displacement)		Disc displacement and bony changes within TMJ	Accuracy Mode!. 99% MRI, bony abnormalities: 60%- 100% MRI, disc position: 73%-85%

Table 3. (Continued)	nued)								
Author, Year	Sample description (age in years and/ or sex)	Study objective	Type of Data used	Algorithms used	TMD subtype studied*	Criteria for diagnosing TMD subtype	Dataset size	Features used for training	Results/Performance
Haghnegahdar et al., 2016 [26]		Local binary patterns for assessment of TMDs	CBCT	Random forest, Naïve Bayes, SVM, KNN, Local binary pattern, Histogram of oriented gradients	TMJOA	clinical examination findings	Training set: 132 Testing set: 132	Condylar shape	KNN a) Accuracy: 92% b) Sensitivity: 94% c) Specificity: 90% SVM a) Accuracy: 84% b) Sensitivity: 84% c) Specificity: 85% Naïve Bayes a) Accuracy: 75% b) Sensitivity: 73% Random forest a) Accuracy: 73% b) Sensitivity: 75% c) Specificity: 73%
de Dumast et al., 2018 [20]		Deep neural network to assess shape changes in TMJOA	CBCT	CNN	TMJOA	morphological variability in radiographs	268 TMJs	Condylar shape	Accuracy Training data: 93% Testing data: 95%
de Dumast et al., 2018 [33]	Mean Age a) TMJOA: 39.9±11.7 b) controls: 39.4±15.4	web-based system for neural network classification of TMJOA	CBCT	CNN, PCA	TMJOA	medical history, clinical examination findings	Training set: 259 Testing set: 34	Serum and salivary biomarkers, condylar shape	PCA a) Pain variables > 82% b) Protein levels in plasma and saliva > 99%
Nam et al, 2018 [31]	 Age: Mean Age TMD: 31.2 ± 15.8 TMD mimicking: 39.5 ± 23.2 Sex: 61 males, 229 females 	NLP to differentiate TMD and TMD mimicking conditions	Medical Records	NLP	TMD (no subtype)	Medical records, RDC/TMD	1	Mouth opening	The goodness-of-fit of the model: 0.643 a) Accuracy: 96.6% b) Sensitivity: 69.0% c) Specificity: 99.3% d) Positive-predictive value: 97.0% e) Negative-predictive value: 97.0%
Ribera et al., 2019 [18]	Mean Age: 39.9± 11.7	Deep neural network to assess bony changes in TMJOA	CBCT	CNN	TMJOA	morphological variability in radiographs	Training set: 259 Testing set: 34	Condylar shape	Accuracy 47% of exact classification (91% for an error of +/-one group)

(Continued)

Table 3. (Continued)	inued)								
Author, Year	Sample description (age in years and/ or sex)	Study objective	Type of Data used	Algorithms used	TMD subtype studied*	Criteria for diagnosing TMD subtype	Dataset size	Features used for training	Results/Performance
Shoukri et al., 2019 [34]	Mean Age a) symptomatic: 39.9±11.7 b) controls: 39.4 ±15.4	Test correlations of biomarkers of condylar morphology and find deep neural network to assess bony changes in TMJOA	hr-CBCT	CNN	TMJOA	Clinical examination findings and radiographic diagnosis based on DC/TMD	Training set: 259 Testing set: 34	Articular fossa and condyle	Predictive analytics of neural network staging of TMJ OA (compared to clinicians' consensus) showing degree of conformity. Training data: 73.5% Testing data: 91.2%
Bianchi et al., 2020 [35]	1.Age Age Range: 21–70 2.Sex: a) CG-7 males, 39 females b) TMJOA-7 males, 39 females	Diagnosis of TMJOA using biomarkers and machine learning	hr-CBCT	Light gradient boosting machine, XGBoost	TMJOA	DC/TMD		Radiomics and biomolecular variables, condylar shape	Accuracy: 0.823 AUC: 0.870 F1 score: 0.823
Bianchi et al., 2020 [36]	1.Agea) Age range- $21-70$ $21-70$ b) Mean ageTMJOA-: 40.2 ± 13.1 controls: 36 ± 11.4 $\pm 2.5 \mathbf{ex}$:a) GG-6 males,33 femalesb) TMJOA-7males, 38femalesfemales	Diagnosis of TMJOA using quantitative bone imaging biomarkers	hr-CBCT	GLCM and GLRLM	TMJOA	DC/TMD	Control group: 39 TMJOA group: 45	Radiomics and biomolecular variables, condylar shape	 ROC curves for variables that presented significant differences between the TMJ OA and control groups Prediction for energy and entropy: AUC > 0.7 AUC for all variables ranged from 0.62 to 0.71
									(Continued)

PLOS ONE

Diagnosis of temporomandibular disorders using AI

	oampie description (age in years and/ or sex)	Study objective	Type of Data used	Algorithms used	TMD subtype studied*	Criteria for diagnosing TMD subtype	Dataset size	Features used for training	Results/Performance
Calif et al., 2020 [27]	1. Age: Age range: 18– 50 2. Sex: a) CG- 5 males, 15 females b) MG-3 males, 7 females c) AG-4 males, 6 females	Analysis of biomechanical features collected by an optoelectronic system to record jaw movements as a diagnostic tool for the evaluation of TMD.	Infrared camera with motion- tracking system	Random forest, Naïve Bayes, SVM, KNN	Myopathy and arthropathy	DC/TMD	1	Protrusion, lateral movements, opening and closing of mouth	KNNN a) Precision: 93%–96% b) Accuracy: 95%–97% c) Sensitivity: 87%–97% d) Specificity: 94%–98% Random forest a) Precision: 66%–79% b) Accuracy: 79%–84% c) Sensitivity: 68%–79% d) Specificity: 79%–84% c) Sensitivity: 76%–94% c) Sensitivity: 76%–94% d) Specificity: 76%–84% d) Specificity: 76%–83% d) Specificity: 77%–79%
Kim et al., 2020 [28]	1. Age: a) Age Range:20-60 b) Average age: 43.3 2. Se x: 700 males, 592 females	Automated detection of mandibular condyle using R-CNN R-CNN	Panoramic radiograph, medical records	CNN	TMJOA	Patient history and clinical symptoms	1.Detection: Training set: 800 Testing set: 167 2.Condyle discrimination: Training set: 2066 Testing set: 518 3. Classification: Training set: 923 Testing set: 231 Testing set: 231	Articular fossa and condyle	Condyle validity classification (Model 2) a) Precision: 93% b) Recall: 83% c) F1 score: 93% Condyle abnormality classification (Model 3): best results shown by VGG16 Fine Tuning a) Accuracy: 84% b) Sensitivity: 54% c) Specificity: 94% d) AUC: 82%
Lee et al., 2020 [17]	1. Age: a) Age range:16–84 b) Mean age:39.5 ± 18.2 2. Sex : 84 males, 230 females	Automated assessment of TMJOA using CBCT images with AI	CBCT	SSD	TMJOA	RDC/TMD	Training set: 1757 Testing set: 300 Validation set:1757	Condylar shape	Accuracy: 0.86 Precision: 0.85 F1 score: 0.85 Recall: 0.84

Table 3. (Continued)

Table 3. (Continued)	nued)								
Author, Year	Sample description (age in years and/ or sex)	Study objective	Type of Data used	Algorithms used	TMD subtype studied*	Criteria for diagnosing TMD subtype	Dataset size	Features used for training	Results/Performance
Kim et al., 2021 [30]	 Age: Median Age a) perforated group: 32 b) non- perforated group: 27 2. Sex: a) perforated group: 10 males, 120 females b) non- perforated group: 30 males, 138 females 	Diagnosis of TMJ disc perforation using deep learning	MRI	MLP (ANN), Random forest	Disc perforation and TMJOA	Criteria defined by author based on MRI (disc shape, joint space, condylar changes)	1	Disc shape, condyle and fossa shape, joint space shape, and bone marrow	MLP showed highest performance a) AUC: 0.940 b) Sensitivity: 85.2% c) Specificity: 84.8% Random forest a) AUC: 0.918 b) Sensitivity: 96.3% c) Specificity: 75.8% Disc shape a) AUC: 0.791 a) AUC: 0.791
Kreiner & Viloria, 2022 [32]		Diagnosis of TMD and orofacial pain using neural networks	Medical records	MIP (ANN)	Internal derangement	Criteria defined by author	1	Questionnaire consisting of symptom onset and description, quality of pain descriptors, pain intensity, time from onset, site & frequency of symptom, aggravating factors etc. comparing ability of MLP and dental practitioners to diagnose clinical cases	diagnostic accuracy of MLP superior to that of clinicians (p = .0072)
*TMD subtype i	s in accordance w	*TMD subtype is in accordance with the Diagnostic Criteria		nporomandibula	r Disorders (DC	for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications [2]	id Research Applic	ations [2]	

Temporomandibular Disorders; F1 score, harmonic mean of precision and recall; GLCM, gray-level co-occurrence matrix; GLRLM, gray-level run-length matrix; hr-CBCT, high resolution CBCT; AUC, area under the curve; BBN, Bayesian belief network; CBCT, cone-beam computed tomography; CG, control group; CNN, Convolutional neural networks; DC/TMD, Diagnostic Criteria for Detector; SVM, support vector machines; TMD, temporomandibular joint disorders; TMJ ID, Temporomandibular joint internal derangement; TMJOA, Temporomandibular joint osteoarthritis. toU, intersection over union; KNN, K-nearest neighbors; MG, myopathy group; MLP, multilayer perception (artificial neural network, ANN); MRI, magnetic resonance imaging; PCA, principal component analysis, PCA, principal component analysis, RDC/TMD, Research Diagnostic Criteria for Temporomandibular Disorders, ROC, receiver operating characteristic; SSD, Single-Shot ADDwoR, anterior disc displacement without reduction; ADDwR, anterior disc displacement with reduction; AG, arthropathy group; AI, artificial intelligence; ANN, Artificial neural network;

https://doi.org/10.1371/journal.pone.0272715.t003

Sex distribution indicated higher number of female subjects than male subjects for most of the studies [17, 21, 27, 30, 31, 35, 36]. Image and nonimage data were used, and medical diagnostic imaging modalities, such as CBCT [17, 18, 20, 26, 33], high-resolution CBCT (HR-CBCT) [34–36], MRI [21, 33], and panoramic radiography [28] were used. Other types of image data included infrared cameras with a motion-tracking system [27] and high-resolution video cameras [19]. Nonimage data included medical records, such as patients' symptoms [25, 29, 31, 32]. The most frequently used method was convolutional neural networks (CNNs; 7 studies), followed by artificial neural networks (3 studies), support vector machines (SVMs; 3 studies), K-nearest neighbors (KNNs; 2 studies), and natural language processing (NLP; 1 study). Some studies used several machine-learning algorithms and compared the results.

Meta-analysis

The diagnostic accuracy was 0.69–1.00, and the pooled accuracy was 0.91 (95% CI 0.76–0.99), $I^2 = 97\%$ (95% CI 0.96–0.98), p < 0.001 (Fig 3). The study with the lowest accuracy had multiple classes of condylar shape in patients with DJD in which the classes represented varying degrees of condylar resorption and remodeling [33].

Discussion

Diagnosis of TMDs can be complex as patients present with various symptoms according to subtypes, thus requiring clinical expertise. Various studies have diagnosed TMDs using AI to facilitate diagnosis and support clinical decisions. However, the accuracy of the developed models varied greatly depending on the type of data used, dataset size, and algorithms used for developing the model.

Among the subtypes of the TMDs, TMJOA was found to be the most studied type of TMD in this systematic literature review. One of the possible reasons is that TMJOA is an advanced form of disease that occurs after disc displacement, and it has a significant effect on occlusion and facial appearance. Deep-learning algorithms were used to diagnose TMJOA by detecting the changes in the condyle shape using CBCT images [18, 20, 33]. Lee et al. developed an automated diagnostic tool for detecting TMJOA based on the Diagnostic Criteria for TMDs [17].

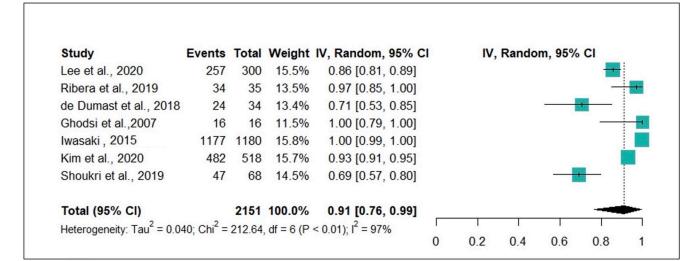


Fig 3. Meta-analysis of seven studies indicated by forest plot.

https://doi.org/10.1371/journal.pone.0272715.g003

Kim et al. used panoramic radiographs to automatically detect the condyles and classify osteoarthritis [28]. Although panoramic radiographs are not considered the standard imaging technique in the diagnosis of TMJOA [4], the AI model showed accuracy, sensitivity, and specificity of 0.84, 0.54, and 0.94, respectively, for diagnosing bony abnormality [28]. Machine-learning methods were used to examine correlations between the biomarkers, and condylar shape changes were investigated to increase diagnostic sensitivity [34–36]. Radiomics features were extracted from high-resolution CBCT scans to detect early bony changes [35, 36].

All studies on TMJOA used image data to analyze mandibular condyle shapes [17-20, 28-31, 33-36], and CBCT was the most commonly used imaging modality. Accurate assessment of bony changes is possible using CBCT; thus, it is considered the gold standard for TMJOA [37]. HR-CBCT scans at a submillimeter resolution with voxel size as low as 80 µm [38]. Compared with micro-CT, it allows observing subtle changes in the trabecular pattern of the condyle [35, 39]. The accuracy of the AI models used in these studies ranged from 80% to 90%, indicating their high reliability. These results are similar to the conventional studies involving human experts to diagnose TMJOA using CBCT [40, 41]. MRI was the most frequently used imaging method for the diagnosis of internal derangements and disc perforations [21, 30]. Other data include jaw movement records [27]. Bas et al. used clinical symptoms and diagnoses to predict the subtypes of internal derangements using ANNs [25]. We provide a brief explanation of techniques used in each study below.

ANN is a popular AI model that includes one input layer, two or three hidden layers, and one output layer. ANN training begins by randomly assigning weights as small numbers near 0 and iterating the feedforward and backpropagation algorithms until certain criteria are met to accurately predict the final output [42].

Deep learning is a subgroup of ANNs that involves many hidden layers. CNNs are a type of deep learning algorithms that have been developed for image data analysis. CNNs can be used for medical image analysis by performing tasks such as classification, which identifies input image data as pretrained classes (such as disease or normal), detection, which locates the region of interest (i.e. abnormal area), and segmentation, which identifies regions of interest as pixel-wise boundaries [43–45].

Decision trees are popular tools that present results in a tree structure that can be easily interpreted, are less time-consuming, and can help understand the interactions among different features [46]. Decision tree algorithms were used by four studies in various forms, such as random forest [26, 27, 30], light gradient boosting machine, and XGBoost [35].

Bayesian networks are a group of techniques connecting statistics and machine learning applicable to complex systems, which can leverage smaller data sizes compared with other machine-learning algorithms [47]. Further, large probability distributions can be compactly represented using Bayesian networks [48]. They comprise factorizing a probability distribution and a corresponding directed acrylic graph (DAG). The DAG presents a cause–effect relation-ship among nodes [21, 48]. Bayesian networks have many forms, including naïve Bayes (supervised classification) [45], greedy search-and-score [21], and Bayesian belief network path condition [21].

SVMs have been recently developed and are useful techniques in pattern recognition and classification studies [49]. Algorithm consideration, i.e., selecting a kernel/learning function, made in advance, can improve the performance of SVMs. This technique involves the nonlinear mapping of input vectors in a high-dimensional feature space to construct a linear decision surface [49].

KNN is one of the simplest classification methods wherein the samples are divided into training and testing groups. Training is performed with known labels, following which test

samples are predicted using the learned model. The training and testing data need not be identical for KNN [50].

NLP is a subfield of AI that is used to decode human language into computer language [31]. Hospital data in the form of clinical history, radiology reports, and physical examination findings are available from clinical databases; these can be interpreted with computational linguistics using AI-assisted NLP systems. Free text can be organized into structured data [31, 51], which reduces labor-intensive and error-prone administrative demands.

Feature extraction techniques such as gray-level co-occurrence matrix, gray-level run-length matrix [36], local binary patterns [26], and histograms of oriented gradients [26] are used as image-processing techniques to automatically analyze texture, shape, and color changes within images. Feature selection is an important step in classification [52]. Different feature extraction algorithms can be sequentially applied to extract feature matrices for individual images. Following this method, feature matrix classification is performed using algorithms, such as SVM and KNN [52]. Principal component analysis (PCA) is a mathematical algorithm used to identify variations in data that simultaneously reduces their dimensionality, creating sample plotting, and identifying similarities and differences within a group of simple tasks [53].

Regarding the risk of bias assessment, this study used the QUADAS-2 tool recommended for systematic reviews of diagnostic accuracy by the Agency for Healthcare Research and Quality, Cochrane Collaboration [54]. We could have used the Cochrane tool for Risk Of Bias due to Missing Evidence in a synthesis. However, this tool was intended for risk of bias assessment for the meta-analyses of the effects of interventions [55]. Some of the included studies showed a high risk of bias in the patient selection domain because they were case-control studies. Other domains showed a low risk of bias and low risk of applicability concerns for all included studies.

Regardless of the possible risk of patient selection bias, most of the included studies reported high performance of the AI models showing a pooled accuracy of 0.91. However, there was a concern about the quality of evidence due to the small number of subjects included in the studies. Moreover, apart from the quality of the evidence, most studies lacked robust validation mechanisms. Validation, i.e., model performance evaluation, may be evaluated using data used for model development (internal) or from separate data that is not used for model development (external) [56]. Crossvalidation or validating from similar data sources may introduce accuracy bias [57]. External validation mechanisms, such as cohort studies, data collection from various institutions, prospective data [58], and data from different sites [56], are needed to improve the accuracy, quality, and generalizability of AI models.

Accuracy of traditional diagnostic tools for TMDs varies greatly. A systematic review on the diagnostic accuracy of clinical diagnostic tests and signs of TMD reported sensitivity and specificity of 2–89% and 14–97%, respectively [59]. The diagnostic accuracy varied according to the disease subtype and diagnostic test and signs used. In contrast, medical imaging modalities such as CT and MRI, which are regarded as gold standards for diagnosis of osteoarthritis and internal derangement, respectively, have shown a high examiner reliability [60]. Latest AI technologies have been introduced to support clinicians in diagnosing TMDs using various types of data, such as medical diagnostic images, video images, radiomics features, jaw movement tracking, electronic medical records (EMR), and biomarkers. These may contribute to the increased diagnostic accuracy.

This study has a few limitations. Most of the included studies have reported the model performance in terms of sensitivity, specificity, accuracy, recall, and R1. However, they did not provide raw data for meta-analysis of sensitivity and specificity, except for one study [14]. Therefore, only accuracy could be calculated in the meta-analysis. Additionally, the accuracies of the included studies showed high heterogeneity because the AI algorithms were developed for different TMD subtypes, thus the number of classes in the output and the criteria for accurate prediction varied among studies. Another limitation is that the study protocol was not registered in PROSPERO, and the transparency of this study could be affected. Lastly, we omitted abstracts and conference proceedings in our review and only used English articles selected from major databases, which collectively may exclude relevant studies published in other languages.

Conclusions

The results of this study suggest that AI algorithms developed for automated TMD diagnosis can be used as a decision support tool for clinicians. In addition to the medical diagnostic images, various input data types, such as EMR, biomarkers, and radiomics features may help increase the diagnostic accuracy of TMDs. However, a high risk of bias in patient selection was present due to the inclusion of case-control studies. Most of the studies used a small training dataset and lacked external validation. Additionally, a significant heterogeneity was observed among the studies included for meta-analysis of diagnostic accuracy. The certainty of evidence was concluded as very low. Further studies with a larger dataset to prevent overfitting and ensure generalizability of developed models are warranted.

Supporting information

S1 Fig. Quality assessment (QUADAS-2) summary table for individual studies. (TIF)

S1 Table. PRISMA 2020 for abstracts checklist. (DOCX)

S2 Table. PRISMA 2020 checklist. (DOCX)

S3 Table. List of excluded studies. (DOCX)

S4 Table. GRADE assessment of the level of evidence for all included studies. (DOCX)

Author Contributions

Conceptualization: Nayansi Jha, Yoon-Ji Kim. Formal analysis: Nayansi Jha, Yoon-Ji Kim. Funding acquisition: Yoon-Ji Kim. Investigation: Nayansi Jha. Methodology: Nayansi Jha, Kwang-sig Lee. Project administration: Kwang-sig Lee, Yoon-Ji Kim. Resources: Nayansi Jha, Kwang-sig Lee. Supervision: Kwang-sig Lee. Validation: Nayansi Jha, Kwang-sig Lee. Writing – original draft: Nayansi Jha.

Writing – review & editing: Kwang-sig Lee.

References

- 1. National Institute of Dental and Craniofacial Research. 2018. Facial Pain and its signs and symptoms [accessed 2021 June 10]. http://nidcr.nih.gov
- Schiffman E, Ohrbach R, Truelove E, Look J, Anderson G, Goulet JP, et al. International RDC/TMDs Consortium Network, International association for Dental Research; Orofacial Pain Special Interest Group, International Association for the Study of Pain. Diagnostic Criteria for Temporomandibular Disorders (DC/TMDs) for Clinical and Research Applications: recommendations of the International RDC/ TMDs Consortium Network and Orofacial Pain Special Interest Group. J Oral Facial Pain Headache. 2014; 28: 6–27.
- 3. de leeuw R, Klasser GD. Orofacial Pain-Guidelines for Assessment, Diagnosis and Management. The American Academy of Orofacial Pain, 2018; 5th ed.
- Schiffman E, Truelove E, Ohrbach R, Anderson G, John MT, List T, et al. The research diagnostic criteria for temporomandibular disorders. I: overview and methodology for assessment of validity. J Orofac Pain. 2010; 24(1): 7–24. PMID: 20213028
- Burris JL, Evans DR, Carlson CR. Psychological correlates of medical comorbidities in patients with temporomandibular disorders. J Am Dent Assoc. 2010; 141: 22–31. <u>https://doi.org/10.14219/jada.</u> archive.2010.0017 PMID: 20045818
- Skog C, Fjellner J, Ekberg E, Häggman-Henrikson B. Tinnitus as a comorbidity to temporomandibular disorders-A systematic review. J Oral Rehabil. 2019; 46: 87–99. <u>https://doi.org/10.1111/joor.12710</u> PMID: 30126027
- Song HS, Shin JS, Lee J, Lee YJ, Kim MR, Cho JH, et al. Association between temporomandibular disorders, chronic diseases, and ophthalmologic and otolaryngologic disorders in Korean adults: A crosssectional study. PLoS One. 2018; 13(1): e0191336. https://doi.org/10.1371/journal.pone.0191336 PMID: 29385182
- McKinney MW, Lundeen TF, Turner SP, Levitt SR. Chronic TM disorder and non-TM disorder pain: a comparison of behavioral and psychological characteristics. Cranio. 1990; 8(1): 40–46. <u>https://doi.org/</u> 10.1080/08869634.1990.11678298 PMID: 2098186
- Esteva A, Kuprel B, Novoa RA, Ko J, Swetter SM, Blau HM, et al. Dermatologist-level classification of skin cancer with deep neural networks. Nature. 2017; 542(7639): 115–118. https://doi.org/10.1038/ nature21056 PMID: 28117445
- Wong TY, Bressler NM. Artificial intelligence with deep learning technology looks into diabetic retinopathy screening. Jama. 2016; 316(22): 2366–2367. https://doi.org/10.1001/jama.2016.17563 PMID: 27898977
- Bhanumurthy MY, Anne K. An automated detection and segmentation of tumor in brain MRI using artificial intelligence. IEEE International Conference on Computational Intelligence and Computing Research; 2014; 1–6.
- Lee JH, Kim DH, Jeong SN, Choi SH. Detection and diagnosis of dental caries using a deep learningbased convolutional neural network algorithm. J Dent. 2018; 77: 106–111. <u>https://doi.org/10.1016/j.jdent.2018.07.015</u> PMID: 30056118
- Machoy ME, Szyszka-Sommerfeld L, Vegh A, Gedrange T, Woźniak K. The ways of using machine learning in dentistry. Adv Clin Exp Med. 2020; 29(3): 375–384. <u>https://doi.org/10.17219/acem/115083</u> PMID: 32207586
- Liao KP, Cai T, Savova GK, Murphy SN, Karlson EW, Ananthakrishnan AN, et al. Development of phenotype algorithms using electronic medical records and incorporating natural language processing. BMJ. 2015; 350: h1885. https://doi.org/10.1136/bmj.h1885 PMID: 25911572
- Ouhmida A, Terrada O, Raihani A, Cherradi B, Hamida S. Voice-Based Deep Learning Medical Diagnosis System for Parkinson's Disease Prediction. International Congress of Advanced Technology and Engineering (ICOTEN). 2021; 1–5.
- Singh SA, Majumder S, Mishra M. Classification of short unsegmented heart sound based on deep learning. 2019 IEEE International Instrumentation and Measurement Technology Conference (I2MTC). 2019; 1–6.
- Lee KS, Kwak HJ, Oh JM, Jha N, Kim YJ, Kim W, et al. Automated Detection of TMJ Osteoarthritis Based on Artificial Intelligence. J Dent Res. 2020; 99(12): 1363–1367. https://doi.org/10.1177/ 0022034520936950 PMID: 32609562
- Ribera NT, de Dumast P, Yatabe M, Ruellas A, Ioshida M, Paniagua B, et al. Shape variation analyzer: a classifier for temporomandibular joint damaged by osteoarthritis. Proc SPIE Int Soc Opt Eng. 2019; 10950: 1095021. https://doi.org/10.1117/12.2506018 PMID: 31359900
- **19.** Ghodsi M, Sanei S, Hicks Y, Lee T, Dunne S. Detection of Temporomandibular Disorder from Facial Pattern. 15th International Conference on Digital Signal Processing, 2007; 151–154.

- de Dumast P, Mirabel C, Paniagua B, Yatabe M, Ruellas A, Tubau N, et al. SVA: Shape variation analyzer. Proc SPIE Int Soc Opt Eng. 2018; 10578:105782H. https://doi.org/10.1117/12.2295631 PMID: 29780198
- Iwasaki H. Bayesian belief network analysis applied to determine the progression of temporomandibular disorders using MRI. Dentomaxillofac Radiol. 2015; 44(4):20140279. <u>https://doi.org/10.1259/dmfr.</u> 20140279 PMID: 25472616
- Page M J, McKenzie J E, Bossuyt P M, Boutron I, Hoffmann T C, Mulrow C D et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews BMJ 2021; 372: n71. https://doi.org/10.1136/bmj.n71 PMID: 33782057
- Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011 Oct 18; 155(8): 529–536.
- Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008; 336(7650): 924–926.
- 25. Bas B, Ozgonenel O, Ozden B, Bekcioglu B, Bulut E, Kurt M. Use of artificial neural network in differentiation of subgroups of temporomandibular internal derangements: a preliminary study. J Oral Maxillofac Surg. 2012; 70(1): 51–59. https://doi.org/10.1016/j.joms.2011.03.069 PMID: 21802818
- Haghnegahdar AA, Kolahi S, Khojastepour L, Tajeripour F. Diagnosis of Temporomandibular Disorders Using Local Binary Patterns. J Biomed Phys Eng. 2018; 8(1): 87–96.
- Calil BC, da Cunha DV, Vieira MF, de Oliveira Andrade A, Furtado DA, Bellomo Junior DP, et al. Identification of arthropathy and myopathy of the temporomandibular syndrome by biomechanical facial features. Biomed Eng Online. 2020; 19(1): 22. https://doi.org/10.1186/s12938-020-00764-5 PMID: 32295597
- Kim D, Choi E, Jeong HG, Chang J, Youm S. Expert system for Mandibular Condyle Detection and Osteoarthritis Classification in Panoramic Imaging Using R-CNN and CNN. Appl Sci. 2020; 10(21): 7464.
- Radke JC, Ketcham R, Glassman B, Kull R. Artificial neural network learns to differentiate normal TMJs and nonreducing displaced discs after training on incisor-point chewing movements. Cranio. 2003; 21 (4): 259–264.
- Kim JY, Kim D, Jeon KJ, Kim H, Huh JK. Using deep learning to predict temporomandibular joint disc perforation based on magnetic resonance imaging. Sci Rep. 2021; 11(1):6680. <u>https://doi.org/10.1038/</u> s41598-021-86115-3 PMID: 33758266
- Nam Y, Kim HG, Kho HS. Differential diagnosis of jaw pain using informatics technology. J Oral Rehabil. 2018; 45(8): 581–588. https://doi.org/10.1111/joor.12655 PMID: 29782036
- Kreiner M, Viloria J. A novel artificial neural network for the diagnosis of orofacial pain and temporomandibular disorders. J Oral Rehabil. 2022. https://doi.org/10.1111/joor.13350 PMID: 35722743
- de Dumast P, Mirabel C, Cevidanes L, Ruellas A, Yatabe M, Ioshida M, et al. A web-based system for neural network based classification in temporomandibular joint osteoarthritis. Comput Med Imaging Graph. 2018; 67: 45–54. https://doi.org/10.1016/j.compmedimag.2018.04.009 PMID: 29753964
- Shoukri B, Prieto JC, Ruellas A, Yatabe M, Sugai J, Styner M, et al. Minimally Invasive Approach for Diagnosing TMJ Osteoarthritis. J Dent Res. 2019; 98(10): 1103–1111. https://doi.org/10.1177/ 0022034519865187 PMID: 31340134
- 35. Bianchi J, de Oliveira Ruellas AC, Gonçalves JR, Paniagua B, Prieto JC, Styner M, et al. Osteoarthritis of the Temporomandibular Joint can be diagnosed earlier using biomarkers and machine learning. Sci Rep. 2020; 10(1): 8012. https://doi.org/10.1038/s41598-020-64942-0 PMID: 32415284
- Bianchi J, Gonçalves JR, de Oliveira Ruellas AC, Ashman LM, Vimort JB, Yatabe M, et al. Quantitative bone imaging biomarkers to diagnose temporomandibular joint osteoarthritis. Int J Oral Maxillofac Surg. 2021; 50(2): 227–235. https://doi.org/10.1016/j.ijom.2020.04.018 PMID: 32605824
- Talmaceanu D, Lenghel M, Bolog N Hedesiu M, Buduru S, Rotar H, Baciut M, et al. Imaging modalities for temporomandibular joint disorders: An update. Clijul Med. 2018; 91(3): 280–287. <u>https://doi.org/10. 15386/cimed-970 PMID: 30093805</u>
- Paniagua B, Ruellas AC, Benavides E, Marron S, Woldford L, Cevidanes L. Validation of CBCT for the computation of textural biomarkers. Proc SPIE Int Soc Opt Eng. 2015; 9417: 94171B. <u>https://doi.org/10.1117/12.2081859</u> PMID: 26085710
- **39.** Bianchi J, Gonçalves JR, Ruellas ACO, Vimort JB, Yatabe M, Paniagua B, et al. Software comparison to analyze bone radiomics from high resolution CBCT scans of mandibular condyles. Dentomaxillofac Radiol. 2019; 48(6): 20190049. https://doi.org/10.1259/dmfr.20190049 PMID: 31075043
- 40. Yadav S, Palo L, Mahdian M, Upadhyay M, Tadinada A. Diagnostic accuracy of 2 cone-beam computed tomography protocols for detecting arthritic changes in temporomandibular joints. Am J Orthod Dentofacial Orthop. 2015 Mar; 147(3): 339–344. https://doi.org/10.1016/j.ajodo.2014.11.017 PMID: 25726401

- Larheim TA, Abrahamsson AK, Kristensen M, Arvidsson LZ. Temporomandibular joint diagnostics using CBCT. Dentomaxillofac Radiol. 2015; 44(1): 20140235 <u>https://doi.org/10.1259/dmfr.20140235</u> PMID: 25369205
- 42. Han J, Kamber M, Pei J. Data mining: concepts and techniques. 3rd ed. Elsevier 2011:744.
- **43.** Kim M, Yun J, Cho Y, Shin K, Jang R, Bae HJ, et al. Deep Learning in Medical Imaging. Neurospine. 2019; 16(4): 657–668 https://doi.org/10.14245/ns.1938396.198 PMID: 31905454
- Soffer S, Ben-Cohen A, Shimon O, Amitai MM, Greenspan H, Klang E. Convolutional Neural Networks for Radiologic Images: A Radiologist's Guide. Radiol. 2019; 290(3): 590–606. https://doi.org/10.1148/ radiol.2018180547 PMID: 30694159
- **45.** Liu W, Anguelov D, Erhan D, Szegedy C, Reed S, Fu C-Y, et al. SSD: Single Shot MultiBox Detector. Cham: Springer International Publishing; 2016; 21–37.
- Stiglic G, Kocbek S, Pernek I, Kokol P. Comprehensive decision tree models in bioinformatics. PLoS One. 2012; 7(3): e33812. https://doi.org/10.1371/journal.pone.0033812 PMID: 22479449
- Becker AK, Dörr M, Felix SB, Frost F, Grabe HJ, Lerch MM, et al. From heterogeneous healthcare data to disease-specific biomarker networks: A hierarchical Bayesian network approach. PLoS Comput Biol. 2021; 17(2): e1008735. https://doi.org/10.1371/journal.pcbi.1008735 PMID: 33577591
- Koski TJ, Noble J. A review of Bayesian networks and structure learning. Mathematica Applicanda. 2012; 40(1).
- 49. Cortes C, Vapnik V. Support-vector networks. Mach Learn. 1995; 20(3): 273-297.
- 50. Bian Z, Vong CM, Wong PK, Wang S. Fuzzy KNN Method With Adaptive Nearest Neighbors. IEEE Trans Cybern. 2020.
- Juhn Y, Liu H. Artificial intelligence approaches using natural language processing to advance EHRbased clinical research. J Allergy Clin Immunol. 2020; 145(2): 463–469. <u>https://doi.org/10.1016/j.jaci.</u> 2019.12.897 PMID: 31883846
- Öztürk S, Akdemir B. Application of Feature Extraction and Classification Methods for Histopathological Image using GLCM, LBP, LBGLCM, GLRLM and SFTA. Procedia Computer Science. 2018; 132: 40– 46.
- Ringnér M. What is principal component analysis? Nat Biotechnol. 2008; 26(3): 303–304. <u>https://doi.org/10.1038/nbt0308-303</u> PMID: 18327243
- Reitsma JB, Rutjes AW, Whiting P, Vlassov VV, Leeflang MM, Deeks JJ. Assessing methodological quality. Cochrane handbook for systematic reviews of diagnostic test accuracy version. 2009 Oct 27; 1 (0): 1–28.
- 55. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011 Oct 18; 343: d5928.
- Park SH, Han K. Methodologic Guide for Evaluating Clinical Performance and Effect of Artificial Intelligence Technology for Medical Diagnosis and Prediction. Radiol. 2018; 286(3): 800–809. <u>https://doi.org/10.1148/radiol.2017171920</u> PMID: 29309734
- Kim DW, Jang HY, Kim KW, Shin Y, Park SH. Design Characteristics of Studies Reporting the Performance of Artificial Intelligence Algorithms for Diagnostic Analysis of Medical Images: Results from Recently Published Papers. Korean J Radiol. 2019; 20(3): 405–410. <u>https://doi.org/10.3348/kjr.2019</u>. 0025 PMID: 30799571
- 58. Farrah K, Young K, Tunis MC, Zhao L. Risk of bias tools in systematic reviews of health interventions: an analysis of PROSPERO-registered protocols. Syst Rev. 2019 Nov 15; 8(1):280 <u>https://doi.org/10.1186/s13643-019-1172-8 PMID: 31730014</u>
- Reneker J, Paz J, Petrosino C, Cook C. Diagnostic accuracy of clinical tests and signs of temporomandibular joint disorders: a systematic review of the literature. J Orthop Sports Phys Ther. 2011 Jun; 41 (6):408–416. https://doi.org/10.2519/jospt.2011.3644 PMID: 21335932
- Ahmad M, Hollender L, Anderson Q, Kartha K, Ohrbach R, Truelove EL, et al. Research diagnostic criteria for temporomandibular disorders (RDC/TMD): development of image analysis criteria and examiner reliability for image analysis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009 Jun; 107 (6):844–860. https://doi.org/10.1016/j.tripleo.2009.02.023 PMID: 19464658