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APPLIED RESEARCH

Assisting in Diagnosis of Temporomandibular Disorders: A Deep Learning Approach

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ABSTRACT The etiology of Temporomandibular disorders (TMD) is still unclear, and its symptoms, signs, and progression are extremely complex. TMD requires early diagnosis and treatments, especially for combinations with other oral diseases. The research targets at developing an artificial neural network (ANN) model for predicting TMD based on clinical-collected data including clinical features, systematic medical condition, and psychosocial state. The popular data mining-based ANN was utilized to predict TMD with all 18 variables collected from patients as the input. The total dataset consists of 88 cases which were reviewed by Board-certificated orthodontists. 75% (66) cases are randomly selected as the training dataset, while the remaining 25% (22) cases are for test. Among the considered 88 cases, 58 (65.9%) were with TMD, while the left 30 (34.1%) without TMD. The numbers of male and female were 21 and 67, respectively, while the average age was 27.63 years. The calculated average sensitivity and specificity of ANN-based TMD risk predictions through 10-fold-cross-validation analysis were 92.31% (95% confidence interval (CI), 62.09%-99.60%) and 88.89% (95% CI, 50.67%-99.42%), respectively. Moreover, the accuracy rate of ANN was 90.91% (95% CI, 78.90%-100.00%). The results show the proposed ANN model could predict the TMD risks with a high accuracy rate, indicating the potential of machine learning in oral and maxillofacial diseases screening and diagnosis, which was further illustrated in a comparison with two doctors. This study can help dental care providers to find individuals' risk of TMD by inputting patient's psychological factors, oral examinations, and systemic medical conditions to the developed artificial intelligence (AI) model.

INDEX TERMS Temporomandibular disorders, machine learning, disease prediction, diagnosis.

I. INTRODUCTION

Temporomandibular joints (TMJ) in front of each ear are one of the most complex joints because of its uniqueness, the only bilateral linkage joints in human body. It mainly consists of articular disc, mandibular condyles, articular surface of the temporal bone, related ligaments, and muscles [1]. Problems with these structures will cause temporomandibular disorders, which are known as TMD. TMD encompasses a subgroup of clinical symptoms of craniofacial pain involving the TMJ, masticatory muscles, and the associated tissues. People with TMD usually have the symptoms of TMJ clicking, pain, and limitations of opening mouth, as well as the comorbid with bruxism, tinnitus, snore, depression, and chronic fatigue [2]. The prevalence is about 31% in adults and 11% in children and adolescents [3], respectively, resulting

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in an estimated annual cost of $4 billions [4]. However, the etiology of TMD remains unclear, and its symptoms, signs, and progression are still complex. Scientists have conducted many researches on the etiology of TMD which includes occlusal elements, muscle dysfunction in oral and maxillofacial areas, biopsychosocial factors, and pathological changes of oral, maxillary, and nervous systems [5]. Even though researchers have reached the consensus that the occlusal abnormality is one of the local biological factors of TMD, it is not the main one [6], [7]. TMD is very complex since the pathogenic factors including behavioral, biological, environmental, social cognitive, and psychological factors can all promote the occurrence of its symptoms.

The Research Diagnostic Criteria for TMD (RDC/TMD) published in 1992 was based on the biopsychosocial model of pain consisting of an Axis I physical assessment and an Axis II assessment of psychosocial status and pain-related disability [8]. Some research works have demonstrated that the primary RDC/TMD biobehavioral measures which are difficult for general dentist without special training course are not complete for the prediction of disease course [9], [10]. The Diagnostic Criteria for TMD (DC/TMD) has been published in [11] and [12] which included vital revisions to the RDC/TMD. The DC/TMD includes important Axis II protocol which adds new tools to assess pain behavior, psychosocial states, and psychosocial functioning. No matter in psychological evaluation, clinical examination items, and diagnostic criteria, DC/TMD classification and diagnostic criteria are simpler and more effective than RDC/TMD. DC/TMD is more suitable for majority of dentists, especially for non-TMD professionals [13]. However, TMD diagnostic criteria is still complex for general dentists in their daily clinical works.

How to improve the diagnostic accuracy of complex diseases has been the research direction of medicine and stomatology. To make a correct diagnosis, expert clinicians have to learn a relatively large number of variables which can define a large variety of diagnoses. For novice physicians in training and non-specialists, they are at higher risks to make inefficient and incorrect decisions [14]. The novice physicians may make the wrong diagnosis of uncommon diseases because of lacking enough clinical experience. During these years of rapid technological development, the emergence of AI technology enables the huge medical data to be integrated into different statistical methods for analysis [15], [16]. After digitizing related factors and symptoms of the diseases, the obtained data can be input to the AI models for complex calculations and conversion, which is termed training. And a function is defined to evaluate the predicted output of the AI models, which is used to guide the training process to learn the features behind the input data. Moreover, if the manual diagnosis corresponding to different symptoms are available, the evaluation function can be defined to measure the gap between the predicted output and manual diagnosis. The training/learning process aiming to minimizing the gap enables the developed AI models to map the relationship between the symptoms and diagnosis. Thus, through learning the relevant medical expertise with AI, clinical thinking and diagnostic reasoning of experts can be simulated. Developing a decision support system is a good way for clinicians to make correct diagnosis and treatment plan.

In 1956, computer scientists first proposed the conception of AI at a Dartmouth conference [17]. As an important branch of computer science, AI has developed rapidly on the basis of electronic computer technology. The concept of AI is that computers and computer-controlled machines perceive and react to their environment and interact with humans based on collected data. And this technology has been widely utilized in the areas of natural language processing, computer vision, intelligent robots, and computer games. More importantly, AI has shown predominant power over human beings in some applications, such as the famous AlphaGo for board games. AI has three kinds of learning manners including supervised learning, unsupervised learning, and reinforcement learning [18]. Supervised learning refers to adjust the AI model and parameters with hand-labeled training data in order to achieve the expected output, while unsupervised learning makes use of unlabeled input data from which the algorithm inferences the structure of interest and conducts the clustering tasks [19]. And these two learning manners have been widely adopted in many medical applications, such as medical image processing, drug discovery, and computer-aided detection and diagnosis system. For example, Anwar Alhazmi et al. developed the Artificial Neural Network (ANN) model based on data of risk factors, medical condition and clinic-pathological features to predict the oral cancer risk [20]. Kim et al. predicted the survival of oral cancer patients by using a deep learning program (Deep Survival) and found this model was superior to that of the classical statistical model [21].

As an important part of the medical field, AI has shown its great advantages in the diagnosis of oral and maxillofacial diseases, the formulation of oral treatment plan, and so on. As TMD is a common disease in the department of stomatology, the AI technique can thoroughly learn its professional knowledge through the continuously iterative analysis of the obtained medical big data including the clinical parameters and imaging examination of patients, which can be further adopted to simulate the manual clinical diagnosis. Thus, in this manuscript, our research wants to use the machine learning to assist the dentists in the actual clinical work to make a correct judgment.

II. RELATED WORKS

In recent years, the emerging techniques in the medical fields have enabled the patient-related big data to be utilized for medical research, among which AI is one of the most promising technologies [18]. The medical application of AI has attracted growing attentions due to its high accuracy rate. As a major branch of medicine, AI has also been playing an increasingly important role in the diagnosis of oral diseases and the formulation of treatment plans [4], [22]. For example, scholars used the Deep Neural Network (DNN)-based image recognition model to diagnose caries, and the accuracy rate of molar region was as high as 88% [23]. In maxillofacial surgery, Alhazmi et al. trained ANN with clinical data of

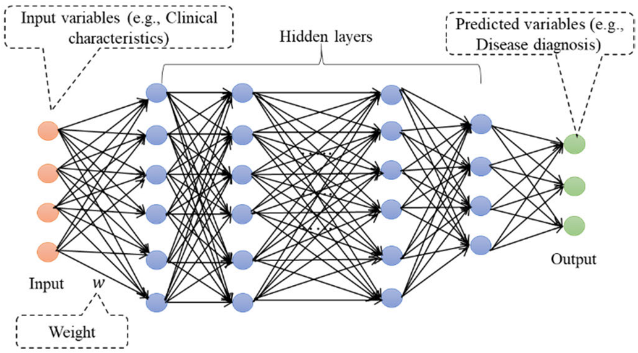

FIGURE 1. A deep learning model (ANN) for disease diagnosis.

oral cancer patients, and the prediction accuracy rate reached 78.95% [20]. Moreover, various AI models have been utilized to classify the normal and osteoporotic subjects, aiming to assist physicians in identifying patients with osteoporosis before implant treatment [24]. In terms of the clinical decision making, the AI-based clinical decision support systems have been developed for the diagnosis of oral and maxillofacial pain [14], the analysis of teeth extraction strategy in orthodontic treatment [25], the automatic identification of the landmark points in cephalometric [26], and the design of removable partial denture in oral prostheses [27].

In the field of TMD, deep/machine learning techniques have been considered to improve the diagnosis systems. Lee et al. [28] utilize the Convolutional Neural Networks (CNN) to detect TMD with the magnetic resonance imaging (MRI), which showed qualified accuracy rate. Luciano et al. [14] reported results of a comparative analysis of the High Frequency Value (HFV) method with other machine learning models as a validation of the dataset creation process and best classification results obtained by using a combination of classifiers for orofacial pain, headache and TMD diagnosis system. In 2020, a study conducted by Jonas et al. [29] also reported that the Extreme Gradient Boosting (XGBoost) + Light Gradient Boosting Machine (LightGBM) model with the features (e. g. clinical features, radiologic characteristics, and biomolecular markers) and interactions achieves the accuracy rate of 0.823 to diagnose the Osteoarthritis of the TMJ. Nam et al. [30] conducted a study where the Natural Language Processing (NLP) methodology was used and the results showed that the frequency of word usage in chief complaint and mouth-opening size could be used to distinguish the TMD-mimicking and genuine TMD groups. Ghodsi et al. [31] adopted the Support Vector Machine (SVM) to classify the TMD subjects and non-TMD subjects according to the movements of markers deployed on the face. [32] gave a comprehensive review on the AI-based TMD diagnosis, in which most of the articles focused on the TMD subtypes.

In the aspect of oral and maxillofacial disease diagnosis [20], ANN as shown in Figure 1 has been used to achieve intelligent and accurate diagnosis by extracting the features of collected clinical parameters and the results of imaging examination and molecular biology examination. An ANN model is composed of the input layer, hidden layer(s), and the output layer, and each layer consists of several neuron units. The neuron units in two adjacent layers are connected by weighted links, which resembles the brain structure. The input data are transmitted and processed mathematically layer-by-layer until the final output layer gives the prediction or classification results. The values of the weights can be adjusted to improve the prediction in the model training process. The simple structure and high accuracy rate of ANN have inspired researchers to utilize it when studying TMD [33], [34]. Kreiner and Viloria [33] adopt ANN to judge TMD according to the orofacial pain. The comparison results with general doctors illustrate that the proposed model can achieve satisfying diagnosis. Lee et al. [34] utilize the six machine learning approaches including ANN to analyze the risk factors of TMD, such as the working conditions, education, region, and so on. ANN has been reported to achieve the highest accuracy rate of 91.11%.

From the above literature review, we can find the proposed CNN-based diagnosis system can achieve qualified accuracy rate to detect TMD [28], but requires the MRI results as input, which poses high expense to the patients and cannot be adopted for many hospital/clinics with no MRI machines. The existing ANN-based research focuses on the analysis of potential effects of environmental factors on the possibility of TMD, instead of the diagnosis system development. To develop the practical doctor-like ANN-based TMD diagnosis system, some important clinical factors including clicking, limited mouth opening, sleep bruxism, and clenching teeth should be considered instead of only the pain symptoms, for the reason that these are highly related factors and commonly asked by the doctors. Moreover, the developed TMD diagnosis system based on the common clinical symptoms asked by the doctors can be more acceptable. In this paper, we hope to develop the ANN-based TMD diagnosis model to imitate doctors, where different data types will be considered to measure the various kinds of TMD symptoms.

III. METHODS AND MATERIALS

A. PATIENT CASES

Before starting the study, the ethical approval (xjkqll [2021] NO.26) has been obtained from the ethics committee, College of Stomatology, Xi'an Jiaotong University on the date of 18th June 2021. A total number of 100 cases with medical records were retrieved. For each case, 18 variables were considered as shown in Table 1. The considered variables except the age and sex have binary values. And the measurement of severity of these symptoms were not considered to avoid and subjectivity and complexity. Moreover, these variables have been verified enough to judge TMD according to experts' experience in this field. The data were first checked manually and clustered. The cases with missing values or abnormal values were considered as noise and removed in the study, while the left 88 cases were fulfilled the eligibility criteria and included in this research, which were described in Supplemental Tables 1 and 2. For each case, eighteen variables were considered to develop the ANN-based prediction model. It should be noted that these variables are chosen after analyzing the practical

TABLE 1. Considered variables to develop the ANN model.

1	Age		
		YES	NO
2	Medical history. Clicking		
3	Medical history. Pain		
4	Medical history. Limitation of mouth opening		
5	Medical history. TMJ with closed lock		
6	Medical history. Dislocation of TMJ		
7	Medical history. Sleep bruxism/Clenching teeth		
8	Medical history. Tinnitus		
9	Medical history. Snore		
10	Medical history. Should pain		
11	Medical history. Neck pain		
12	Medical history. Back pain		
13	Medical history. Upper limb pain		
14	Medical history. Lower limb pain		
15	Medical history. Pretragal pain		
16	Medical history. Head tilt dysfunction		
17	Medical history. Knee joint pain		
18	Special examination. Occlusal interference		

TMJ: Temporal-mandibular joint

clinical records and they have been widely considered in the diagnosis of TMD. The dataset was randomly spilt into the training group and testing group consisting of 66 (75%) and 22 (25%) cases, respectively. All records and observations were reviewed by board-certified orthodontists.

B. MOTIVATIONS TO UTILIZE ANN

According to the above discussion on existing research, it can be found that ANN is one of the most commonly utilized models for disease detection and diagnosis for the reason that it is uncomplicated and robust. Moreover, ANN is suitable and efficient to extract the features behind the collected data which belong to different clinical symptoms. Therefore, this architecture is considered in this research. And the proposed ANN model can learn the key features behind the data through training process and output the degree of certainty according to the input variables in the prediction process [35]. These merits enable ANN to be applied in many medical applications.

C. FORMULATION OF THE ANN MODEL

The developed model consisted of the input and output layers as well as two hidden layers. The input layer was composed by 18 artificial neurons which were corresponding to the 18 features considered to judge TMD in each case. The binary values, 1 and 0, were assigned for each symptom to denote "Yes" and "No", respectively. Moreover, the sex was also assigned 1 and 0 to denote female and male. For the variable of age, we utilized the maximum values for normalization. Then, the values of these variables were input to the first layer of the constructed model. The numbers of hidden layers and neurons in each hidden layer were decided through the training process, while the Rectified Linear Unit (ReLU) function was chosen as the activation function [36]. The formula of ReLU was given as below:

$$y_j = max\left(0, \sum_i w_{ij}x_i + b_j\right) \tag{1}$$

TABLE 2. Parameters of ANN.

Layer	Number of neuron units	Activation function
Input layer	18	No
Hidden layer 1	6	ReLU
Hidden layer 2	4	ReLU
Output layer	2	Softmax

where x_i denoted the i^{th} neuron unit in last layer. y_j was the j^{th} neuron in each hidden layer, and b_j represented its bias. w_{ij} denoted weight of the connection between the i^{th} neuron in last layer and j^{th} neuron in current hidden layer. Since ReLU is a fragmented function, different data samples would get different conversion according to where the values located.

For the output layer, two artificial neurons and the softmax activation functions were considered as there were two kinds of diagnosis results, positive or negative. The softmax had been demonstrated highly efficient if the results were mutually exclusive [37], of which the formula was given as below:

$$\text{softmax}\,(z_i) = \frac{e^{z_i}}{\sum_j^n e^{z_j}} \tag{2}$$

where z_i and z_j denoted the weighted values of i^{th} and j^{th} neurons in the final layer. n was the number of categories in the results, here $n = 2$ in the research.

The final output could be [0, 1] or [1, 0] to represent positive or negative, respectively. We adopted Python 3.8 and Tensorflow to construct the ANN model, while the following training and testing process were run in the software of PyCharm Edu.

D. TRAINING AND VALIDATING PROCESS

The model was trained for 450 iterations, after which the prediction loss function converged. And in each iteration of the training process, the 10-fold cross-validation was preformed meaning that the randomly selected 10% of total training samples were used to validate the ANN model trained with the left 90%. In this way, the limited training data samples could be efficiently utilized to optimize the parameters of the considered ANN model.

After training, the final ANN architecture consists of one input layer, two hidden layers, and one output layer. The number of neurons units and activation function of each layer could be found in Table 2. The weight values could be easily obtained by reconstructing the ANN model according to the provided parameters and training data.

E. TESTING PROCESS

The performance of the ANN-based TMD prediction model was evaluated through the metrics of sensitivity, specificity, and accuracy tests, which have been commonly used for statistics. Thus, the 18 variables of the test dataset were first input to the trained ANN and the predicted output was compared with the corresponding labeled output to calculate the four metrics including True Positive (TP), True Negative (TN), False Positive (FP), and False Negative (FN). Here,

TABLE 3. Summary of utilized dataset.

Total samples (88)	TMD	58
	Without TMD	30
	Male	21
	Female	67
	Average age (year)	27.63
Training samples (66)	TMD	45
	Without TMD	21
	Male	15
	Female	51
	Average age (year)	28.80
Testing samples (22)	TMD	13
	Without TMD	9
	Male	6
	Female	16
	Average age (year)	24.14

TABLE 4. Prediction result of data set.

Statistic	**Value**	**95% CI**
Sensitivity	92.31%	62.09%-99.60%
Specificity	88.89%	50.67%-99.42%
Positive likelihood Ratio	8.31	1.30-53.07
Negative likelihood Ratio	0.09	0.01-0.58
Positive Predictive Value	92.30%	62.09%-99.60%
Negative Predictive Value	88.89%	50.67%-99.42%
Accuracy	90.91%	78.90%-100.00%

TP and TN represent the ANN model can correctly predicts the positive and negative cases, respectively. Otherwise, FP and FN denote the incorrect predictions of positive and negative cases, respectively.

IV. RESULTS

In this research, the total number of considered cases was 88, of which 58 (65.9%) were cases with TMD, while the left 30 (34.1%) were cases without TMD. Twenty-one were male, sixty-seven were female, with an average age of 27.63 years. And Table 3 lists the sample characteristics used for training and testing. All 18 variables used to develop the ANN model are shown in Table 1.

After the training process, we utilized the data in the testing group to evaluate the accuracy rate. The data in the testing group were new for the constructed ANN model. For the pooled accuracy, the sensitivity and specificity were calculated with the predicting results of testing group obtained by Youden Index [28]. With the data in the testing group, the prediction results of four values including true positive, true negative, false positive, and false negative were 12, 8, 1, and 1, respectively. Thus, our analysis (Table 4) illustrated that the values of average sensitivity and specificity for the ANN-based TMD risk prediction model through 10-fold-cross-validation analysis were 92.31% (95% confidence interval (CI), 62.09%-99.60%) and 88.89% (95% CI, 50.67%-99.42%), respectively. And the ANN can achieve an accuracy rate of 90.91% (95% CI, 78.90%-100.00%) in the TMD predictions.

From Table 4, it could be found that the accuracy rate of proposed ANN model was very high. Moreover, the high sensitivity and specificity mean that the proposed model could accurately distinguish the TMD patients and non-TMD patients. We could also compare the results with existing TMD-related research [28], [29], [34]. We could find the ANN model could achieve the accuracy rate of 92.31%, which was much higher than the CNN model [28] and XGBoost+LightGBM [29] with the accuracy rates of 76.92% and 82.3%, respectively. The ANN also had lower expense as the variables in the input were easily to be obtained. The ANN model in [34] also achieved the accuracy rate of more than 90%. However, this study focused on the effects of potential environmental factors on the possibility of TMD, instead of the TMD diagnosis system.

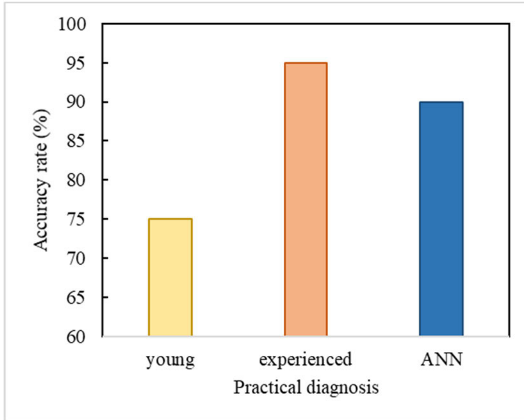

FIGURE 2. Practical TMD diagnosis test for a young doctor, an experienced doctor, and the proposed ANN model.

To further evaluate the effectiveness of the proposed model in practical diagnosis, a comparison experiment with two doctors majoring in the oral and maxillofacial diseases was conducted. In the experiment, another 20 patients' data as shown in Supplementary Table 3 were utilized. And among these 20 patients, 17 were with TMD, while the remaining 3 without TMD. To guarantee the accurate diagnosis, the diagnosis results had been confirmed with the MRI, even though this manner was not usually for the practical diagnosis. To ensure the fairness, a doctor with experience of more than 20 years and a doctor who had worked in this field for only 2 years were selected at the same time. The dataset in Supplementary Table 3 were offered to the two doctors after their labels were deleted. And the two doctors were asked to judge whether the patients have TMD or not according to the personal information and clinical symptoms. The results were compared with the practical labels which were shown in Figure 2.

In the experiment, the prediction accuracy rate of ANN was 90%, while the accuracy rates of the experienced doctor and the young doctor were 95% and 75%, respectively. It could be found that the accurate rate of the proposed ANN was just slightly smaller than the experienced doctor, but much higher than the less experienced doctor. Since the experienced doctors were usually limited in each hospital, the proposed ANN could provide important assistance to doctors in practical diagnosis, especially for the young and new doctors. Moreover, for most general hospitals, there was no separate oral and maxillofacial surgery, especially for developing countries. In this case, the proposed AI-based model could easily help the doctors to find the TMD patients.

V. DISCUSSION

TMD refers to a group of clinical conditions characterized by pain and/or dysfunction in the masticatory muscles and/or the TMJs. TMD is presented by reginal pain, especially in the facial area, and limited mandibular movement. As an important health problem, the prevalence of TMD reached approximately 31% and 11% for elderly and children, respectively [3]. Since hormonal, physical, and psychosocial changes are high risks for TMD, it is more prevalent in young and middle-aged females [38]. In this study, an ANN model was developed to estimate the TMD risk according to the clinical dataset including eighteen variables. The performance analysis illustrated high accuracy rate, sensitivity, and specificity.

Moreover, the ANN model is easy to be developed since the data just need to be normalized before training process. And the features behind the data can be automatically extracted by the training process, meaning that no human intervention is needed, which is much more convenient than the machine learning models utilized in existing TMD-related research [14], [30]. The challenge is how to adjust the numbers of hidden layers and neuron units in each hidden layer of the ANN model. And the training of ANN can easily fall in the trap of under learning or over learning if the hidden layer consists of too many or few neurons, resulting in the low prediction accuracy rate. Fortunately, these parameters can be optimized by computer programming. Another key issue to decide the performance of ANN is the distribution of considered training data. If the training dataset is unbalanced meaning that some certain feature is under/over-represented, the trained ANN model can easily overfit the features. Thus, the developed model is not generalized and may mislead the doctors to make incorrect diagnosis for the patients with certain features. Therefore, when developing the ANN model for disease diagnosis, we should collect large-sized dataset to cover all the potentially relate features as well as the linear or non-linear dependencies. Once the dataset is not very large but balanced, some techniques such as the k-fold training utilized in this study can be considered to improve the utilization efficiency.

For the proposed ANN model in this paper, we consider 18 variables of patients including the physiological information and clinical symptoms. Compared with the research [31], we consider more comprehensive information instead of only orofacial pain. As the orofacial pain can be caused by many oral and maxillofacial diseases, taking the symptoms such as clicking, tinnitus, and snore can significantly improve the accuracy rate. Moreover, this model does not utilize MRI as input, which is more cost-effective and easily to be applied compared with [28]. Furthermore, the proposed model aims to assist the doctors for the diagnosis of TMD instead of study the potential risks behind TMD [34].

As retrospective research, the performance of current research is constrained by the limited training dataset. Current data can only cover patients from limited sites, while the collected diagnosis is from a few experts. And the difficulty of the juveniles in communicating with doctors may result in some unreliable data. These factors may decrease the Certainty of Evidence (CoV). In the future we should reach more patients from various sites and collect more clinical data. Then, future proposed AI models trained with bigger dataset can better extract the features of the diseases and more accurately predict the progression, as well as improve the CoV.

VI. CONCLUSION

In this paper, we designed an ANN-based TMD diagnosis system with the symptoms commonly asked by the doctors as the input. The results indicated the proposed ANN model could perform well in the TMD risks predictions. The high accuracy rate of the proposed ANN-based TMD risks predicting model demonstrated the potential of machine learning to assist oral and maxillofacial diseases screening and diagnosis. Thus, the proposed ANN model in this article could enable dental care providers to find the individual's risk of TMD according to the patients' phycological factors, oral examinations, and systemic medical conditions. As the input consisted of the common symptoms of TMD patients which could be easily obtained by the doctors, the proposed diagnosis symptom was more acceptable. In the future, more variable forms of data including patient's clinical parameters, medical imaging, and biomarkers can be collected to increase the accuracy rate and efficiency of the developed AI models for TMD screening and diagnosis.

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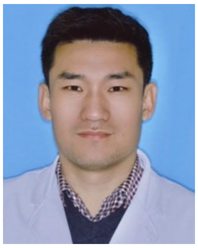

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