

A decision support system for primary headache developed through machine learning

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Background: Primary headache is a disorder with a high incidence and a low diagnostic accuracy; migraine and tension-type headache rank first in incidence among the types of primary headache. Artificial intelligence (AI) decision support systems have shown great potential in the medical field. Therefore, we used machine learning to build a clinical decision-making system for primary headache. **Methods:** The demographic data and headache characteristics of 173 patients were collected by questionnaire. Decision tree, random forest, gradient boosting and support vector machine (SVM) models were used to construct a discriminant model, and a confusion matrix was used to calculate evaluation indicators of the models. Furthermore, we have carried out feature selection through univariate statistical analysis and machine learning. **Results:** In the models, the accuracy, F1 score were calculated through the confusion matrix. The logistic regression model had the best discrimination effect, with the accuracy reaching 0.84 and the area under the ROC curve being the largest among the models, at 0.88. Furthermore, we identified the most important factors for distinguishing the two disorders through statistical analysis and machine learning: nausea/vomiting and photophobia/phonophobia. These two factors represent potential independent factors for the identification of migraines and tension-type headaches. **Conclusions:** Applying machine learning to the decision-making system for primary headache can achieve high diagnostic accuracy. Among the investigated models, the integrated algorithm achieved a significantly better discrimination effect than the single learner methods. In addition, nausea/vomiting and photophobia/phonophobia may be the most important factors for distinguishing migraines from tension-type headaches.

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10

11 Abstract

12 **Background :** Primary headache is a disorder with a high incidence and low diagnostic

13 accuracy; the incidence of migraine and tension-type headache ranks first among primary

14 headaches. Artificial intelligence (AI) decision support systems have shown great potential in the

15 medical field. Therefore, we attempt to use machine learning to build a clinical decision-making

16 system for primary headaches.

17 **Methods :** The demographic data and headache characteristics of 173 patients were collected

18 by questionnaires. Decision tree, random forest, gradient boosting algorithm and support vector

19 machine (SVM) models were used to construct a discriminant model and a confusion matrix was

20 used to calculate the evaluation indicators of the models. Furthermore, we have carried out

21 feature selection through univariate statistical analysis and machine learning.

22 **Results :** In the models, the accuracy, F1 score were calculated through the confusion matrix.

23 The logistic regression model has the best discrimination effect, with the accuracy reaching 0.84

24 and the area under the ROC curve also being the largest at 0.88. Furthermore, we identified the

25 most important factors for distinguishing the two disorders through statistical analysis and

26 machine learning: nausea/vomiting and photophobia/phonophobia. These two factors represent
27 potential independent factors for the identification of migraines and tension-type headaches.

28 **Conclusions** : Applying machine learning to the decision-making system for primary headaches
29 can achieve a high diagnostic accuracy. Among them, the discrimination effect obtained by the
30 integrated algorithm is significantly better than that of a single learner. Second, nausea/vomiting,
31 photophobia/phonophobia may be the most important factors for distinguishing migraine from
32 tension-type headaches.

33 **Introduction**

34 Headache is one of the most common symptoms in neurology clinics. More than 90% of the
35 general population reports suffering from headache during any given year, which can be regarded
36 as a lifetime history of head pain [1]. In China, the 1-year prevalence of primary headache is
37 reported to be 23.8%. The prevalence of migraine was 9.3%, and that of tension-type headaches
38 was 10.3% [2]. Due to the massive population base, patients spend 672.7 billion yuan each year
39 - - because of primary headaches, accounting for 2.24% of China's GDP [3]. Although headaches
40 do not seriously threaten the lives of patients, they can severely affect their work and quality of
41 life, cause them to withdraw from society, and place heavy burdens on the patients' psychology,
42 physiology and the families of patients as well as China's national economy [4-6].

43 Headaches are divided into primary headaches and secondary headaches. There are many causes
44 of headaches. Due to the similarity of symptoms, it is easy for general practitioners to miss or
45 misdiagnose the type of headache. Furthermore, the International Headache Society (IHS) released
46 the latest headache classification in January 2018, which is the International Classification of
47 Headache Disorders (ICHD-III) [7], which lists more than 200 headache variants. This
48 complicated classification creates a very challenging task for general clinicians. There is no

49 objective gold standard, which contributes to the difficulty of diagnosing and classifying
50 headaches. In addition, because the medical community has generally not paid enough attention to
51 headaches in clinical practice for a long time, the proficiency level of clinicians regarding the
52 headache classification is uneven. For example, "vascular headache" and "nervous headache" are
53 still used to diagnose primary headache.

54 Thus, much progress remains to be made toward standardizing and improving the accuracy of the
55 clinical diagnosis of headache.

56 According to reports, primary headaches occur more frequently than secondary headaches, and the
57 incidence of migraine and tension-type headache ranks first among the types of primary headache
58 [8]. Migraines include migraines with aura and migraines without aura. Migraines without aura
59 are typically unilateral, pulsating, and moderate to severe headaches; daily physical activity can
60 exacerbate these headaches, and they are often accompanied by nausea/vomiting and/or
61 photophobia/phonophobia. Aura is the gradual appearance of visual, sensory, or other central
62 nervous system symptoms before or during the headache. Tension-type headaches are the most
63 common type of primary headache; attacks of this type of headache are not frequent and usually
64 last several minutes to several days. These headaches are typically characterized by mild to
65 moderate bilateral compression or band-like sensation; they are not aggravated by daily physical
66 activity and are not often accompanied by nausea/vomiting, or photophobia/phonophobia.
67 Although there are large differences between typical migraines and tension-type headaches, the
68 symptoms of most patients are not typical, especially in cases of tension-type headache and
69 migraine without aura. Thus, it is often difficult to distinguish between them. Due to the many
70 differences in the treatment of the two disorders, misdiagnosis and missed diagnosis inevitably
71 delay the appropriate treatment of the patients[9].

72 At present, the development of Artificial Intelligence (AI) is in full swing. Automatic classifiers,
73 which are faster than clinicians due to their ability to analyze massive amounts of medical data,
74 can minimize errors in disease recognition and improve diagnostic accuracy. Support vector
75 machine (SVM) models, random forests, etc. have been used in the diagnosis of heart disease [10],
76 breast cancer [11], prostate cancer [12], Alzheimer's disease [13], and many other diseases. The
77 future of AI in neurology is promising, with potential applications ranging from the prediction of
78 outcomes of seizure disorder [14], the grading of brain tumors [15], the upskilling of neurosurgical
79 procedures [16], and the rehabilitation of stroke patients to the use of smartphone apps for
80 monitoring patient symptoms and progress [17].

81 For the proper recognition of headache, high-quality computer software could be very useful. As
82 early as 2013, Bartosz et al proposed the automatic diagnosis of primary headaches through
83 machine learning. The comparison of diagnostic performance between the advanced machine
84 learning technology and clinicians revealed that the computer decision support system achieved a
85 higher diagnostic accuracy [18]. More recently, Gilles et al proposed an end-to-end decision
86 support system to improve the efficiency of diagnosis and follow-up in the treatment of primary
87 headaches. The decision support system includes three large components and a shared backend: a
88 mobile application for patients, a web application for doctors to visualize the collected data, and
89 an automatic diagnosis module. In the automatic diagnosis module, a decision tree is used for
90 modeling [19]. Yin et al proposed a primary headache decision-making system based on
91 international headache diagnostic criteria and conducted a four-month clinical evaluation at the
92 International Headache Center of a tertiary hospital in Beijing. Good results have been obtained
93 in terms of the sensitivity and specificity of this system for diagnosing headaches [20].
94 Considering the incomplete language rules when human experts express their knowledge,

95 Monire et al improved the algorithm and used the Learning-From-Examples (LEF) algorithm to
96 train the diagnostic fuzzy system, and the correct recognition rate reached 85%. They further
97 proposed SVM- and multilayer perceptron (MLP)--based decision support systems, which
98 achieved accuracy rates of 90% and 88%, respectively [21]. Simi'c et al create a hybrid
99 intelligent system for diagnosing primary headache disorders, applying various mathematical,
100 statistical and artificial intelligence techniques[22]. Although various types of research have been
101 devoted to computer decision support systems, there are still major obstacles to their widespread
102 use in clinical practice. Machine learning applied to medical records can be an effective tool to
103 predict disease. In China, machine learning methods for diagnosing primary headache remain
104 lacking.

105 Therefore, to achieve a higher headache diagnostic accuracy, we collected information from
106 primary headache patients in neurology clinics through questionnaires and then entered the data
107 into the system. We compared various machine learning algorithms to identify the best model.
108 Furthermore, through feature selection, we identified the most important factors for distinguishing
109 migraines from tension-type headaches, which provide a basis for clinicians to quickly diagnose
110 headaches.

111 **Materials & Methods**

112 This is a cross-sectional study designed to obtain a diagnostic discriminant model for migraines
113 and tension-type headaches and to screen out the most important factors for distinguishing the two.
114 The study was approved by the Ethics Committee of the Ninth People's Hospital affiliated to
115 Shanghai Jiao Tong University Medicine (approval no.SH9H-2021-T72-1), and met the
116 requirements of the Declaration of Helsinki. Eligible patients were patients diagnosed with
117 headaches between October 2019 and September 2020 at the Department of Neurology, Shanghai

118 Ninth People's Hospital. All the patients were residents of China. Before the study, we obtained
119 signed informed consent from the participating patients. Two weeks after a patient's questionnaire
120 was collected, we followed up on the patient's headache improvement to further verify the
121 diagnosis. Finally, we included 173 patients with a definite diagnosis of primary headache (84
122 patients with migraine headaches and 89 patients with tension-type headaches) for research.

123 **Data acquisition**

124 First, we designed a paper questionnaire for the outpatients to complete. The questionnaire
125 included a total of 19 questions to collect the demographic data (age, sex, occupation, height, and
126 weight) on the patients and their headache characteristics (course, duration, nature, location, severe
127 intensity, accompanying symptoms, triggers, alleviative methods, and whether activity aggravates
128 the headache). After analysis and modification of the questionnaire by three experienced
129 neurologists, the questionnaire was deemed effective for collecting patient-related information,
130 and the data obtained were reliable to a certain extent.

131 Furthermore, information on related examinations and MRI were used to rule out the patient's
132 secondary factors. Three neurologists were invited to make a diagnosis for each patient based on
133 the questionnaire information we collected. Based on both the diagnosis and the follow-up results,
134 each patient was accurately diagnosed. Due to the low proportion of primary headaches such as
135 neuralgia and cluster headaches among the collected observations, we excluded these rare types of
136 headaches to reduce the problems caused by sample imbalance. Ultimately, 173 patients (84
137 patients with migraines and 89 patients with tension-type headaches) were included in the study
138 (Fig1). Each patient's headache may have had multiple natures or been accompanied by multiple
139 symptoms. Therefore, we performed a binary classification of the collected data and obtained a
140 total of 48 variables. Considering that the incidence of many variables was extremely low, we first

141 identified 10 variables with statistically significant differences between migraines and tension-
142 type headaches. After data transformation and data reduction, the data sheet used to acquire data
143 during the clinical interview is shown in Table 1.

144 **Discriminant model establishment**

145 Using the above 10 feature variables, we randomly divided the entire dataset into a training set
146 and a test set at several ratio variations (60:40, 70:30, 80:20) and used holdout and cross-
147 validation methods to build the primary headache discriminant models. Data analysis was
148 performed in Python (version 3.6.1). We used the decision tree, random forest, gradient boosting,
149 logistic regression, and SVM algorithms to construct discriminant models.

150 Decision tree

151 Decision tree is a nonparametric supervised learning method. The basic idea is to separate binary
152 variables and construct a tree that can be used to predict the category of new variables. It
153 traverses the training data and condenses the information into the internal nodes and leaf nodes.
154 Firstly, it summarizes decision rules from a series of data with features and labels, then present
155 these rules in a tree structure to solve classification problems.

156 Random forest

157 Random forest is an integrated algorithm that completes the learning task by constructing and
158 combining multiple learners. These learners are always classification trees. Firstly, the data is
159 classified by all trees, then the new category is determined by the majority decision principle. It
160 is nonparametrically interpretable and compatible with many types of data, with high prediction
161 accuracy.

162 SVM

163 SVM is a binary supervised classification method, which shows many unique advantages in
164 solving small sample, nonlinear and high-dimensional pattern problems. The purpose of this
165 method is to find an optimal decision boundary in a multidimensional space, which can
166 maximize the distance between two closest points in different categories. This method can
167 process various types of data. From an academic point of view, SVM may be the closest machine
168 learning algorithm to deep learning.

169 Gradient boosting

170 Gradient boosting is another integrated algorithm. Like random forest, it constructs multiple
171 learners and brings them together into a final summed prediction. The main advantage of this
172 method is that can process various types of data flexibly, including continuous values and
173 discrete values.

174 Logistic regression

175 Logistic regression is a supervised learning algorithm to solve the binary classification problem,
176 which is used to estimate the probability of a certain category. It also can process various types
177 of data.

178 Furthermore, we combined the accuracy and F1 score as evaluation indicators of the model
179 through the common confusion matrix, and then measured the prediction result (receiver operating
180 characteristic, ROC) curve and the area under the ROC curve. The F1 score is the harmonic mean
181 of the precision and recall. It is used in statistics to measure the accuracy of two classifications and
182 assume that recall and precision are equally important.

183
$$F1 \text{ score} = \frac{2\mathbf{Precision} * \mathbf{Recall}}{\mathbf{Precision} + \mathbf{Recall}}$$

184 **Feature selection**

185 The ten variables have redundancies in terms of allowing clinicians to quickly distinguish whether
186 a headache is a migraine or tension-type headache. Therefore, we identified the two variables that
187 are most meaningful for diagnosing migraines and tension-type headaches through feature ranking.
188 First, we adopted traditional univariate biometric analysis and then performed machine learning
189 analysis. For the univariate test, we used the Pearson correlation coefficient (PCC) [20], and the
190 chi-square test to compare each feature between the two groups. The PCC represents the linear
191 correlation between the elements of the two lists. If the elements in the two lists are linearly
192 correlated, the absolute value of the PCC will produce a high value close to 1; otherwise, it will be
193 close to 0. The chi-square test is applied to two features to observe the probability of the
194 distribution occurring by chance. Each feature tested will produce a p-value. Although the P-value
195 does not represent the strength of the relationship between the two variables, it provides an
196 indication: the lower the p-value is, the greater certainty that the two variables are related.
197 Furthermore, we ranked the feature importance with the random forest method. The random forest
198 model is a nonlinear decision tree combination model. It is easy to implement and has superior
199 performance. It was once known as "the method that represents the level of integrated learning
200 technology". Using the random forest algorithm for feature selection is superior to the use of linear
201 discriminant analysis and mean squared error methods for eliminating redundant features. The
202 main idea is to judge how much each feature contributes to each tree in the random forest and then
203 to take the average value and evaluate the contribution of each feature separately. Compared with
204 the PCC, the random forest is more capable of mining the deep correlation of data features.

205 **Results**

206 **Patient baseline characteristics**

207 In our study, we enrolled 300 patients with primary headache. A total of 103 patients were
 208 excluded according to the exclusion criteria. In addition, 24 patients were not followed up within
 209 2 weeks (Fig 1). Finally, we included 173 patients (84 patients with migraines and 89 patients with
 210 tension-type headaches). We randomly divided the data from these 173 patients into a training set
 211 and test set at several ratio variations (60:40, 70:30, 80:20). Our questionnaire collected
 212 information on 48 patient characteristics through 19 questions. We used the chi-square test to
 213 identify 10 informative characteristics and included them in the study (Table 1).

214 **Table 1** Patient baseline characteristics

Characteristics	Migraine (n=84)	Tension-type headache (n=89)	Total	P-value
Sex/n(%)	-	-	-	-
Female	20(23.8)	39(43.8)	59(34.1)	P=0.01
Male	64(76.2)	50(56.2)	114(65.9)	
Course/n(%)				
Year	11(13.1%)	38(42.7%)	49(28.3)	P < 0.001
Month	73(86.9%)	51(57.3%)	114(65.9)	
Throbbing/n(%)				
Yes	17(20.2)	6(6.7)	23(13.3)	P=0.01
No	67(79.8)	83(93.3)	150(86.7)	
Occiput/n(%)				
Yes	22(26.2)	43(48.3)	65(37.6)	P=0.00
No	62(73.8)	46(51.7)	108(62.4)	
Severe intensity/n(%)				
Light	13(15.5)	30(33.7)	43(24.9)	P < 0.001
Medium	44(52.4)	51(57.3)	95(54.9)	
Heavy	27(32.1)	8(9.0)	35(20.2)	
Nausea/ vomiting /n(%)				
Yes	44(52.4)	16(18.0)	60(34.7)	P < 0.001
No	40(47.6)	73(82.0)	113(65.3)	
Photophobia/ phonophobia /n(%)				
Yes	27(32.1)	4(4.5)	31(17.9)	P < 0.001
No	57(67.9)	85(95.5)	142(82.1)	
Spark/n(%)				
Yes	11(13.1)	3(3.4)	14(8.1)	P=0.02
No	73(86.9)	86(96.6)	159(91.9)	
Change after activities/n(%)				
Aggravate	41(48.8)	18(20.2)	59(34.1)	P < 0.001
Unchanged	38(45.2)	62(69.7)	100(57.8)	
Relieve	5(6.0)	9(10.1)	14(8.1)	
Alleviative methods/n(%)				
Persistence	9(10.7)	14(15.7)	23(13.3)	P=0.00
Rest	25(29.8)	45(50.6)	70(40.5)	

215	Drug	48(57.1)	25(28.1)	73(42.2)
	Else	2(2.4)	5(5.6)	7(4.0)

216

217 **Model building**

218 For the above 10 feature variables, we used the decision tree, random forest, gradient boosting,
 219 logistic regression, and SVM algorithms to construct the discriminant models. The accuracy, F1
 220 score were calculated through the confusion matrix (Table 2), the discrimination result curve (ROC
 221 curve) was constructed, and the area under the ROC curve were measured (Fig 2). The accuracy
 222 of the decision tree is 0.72, which was significantly lower than that of the integrated learning
 223 algorithm and SVM models. The random forest, gradient boosting algorithm, and SVM models
 224 have similar discrimination effects; their accuracy scores were 0.80, 0.79, and 0.82, and the areas
 225 under the ROC curves were 0.85, 0.82, and 0.82, respectively and the F1 score were 0.79, 0.79,
 226 and 0.81, respectively. Logistic regression had the best discrimination effect, with the accuracy
 227 reaching 0.84 and the area under the ROC curve also being the largest among the methods, at 0.88.
 228 The discrimination effect achieved by the integrated algorithm was better than that of a single
 229 learner method, and among the models, logistic regression achieved the best discrimination effect.

230

Table 2 Evaluation of the discriminant effect of various models

	Accuracy	F1-score	ROC-AUC
Decision tree	0.72	0.68	0.72
Random Forests	0.80	0.79	0.85
Gradient boosting	0.79	0.79	0.82
Logistic regression	0.84	0.83	0.88
SVM-linear	0.82	0.81	0.82

231

232 **Feature selection**

233 For feature selection, we applied two methods: univariate statistical analysis and machine learning.
 234 For the univariate test, we used the PCC (Fig 2) and the chi-square test (Table 3) to compare each
 235 feature between the two groups and rank them according to p-value. Through the univariate chi-

236 square tests, we determined that the smallest p-values were obtained for the variables indicating
237 whether the headache was accompanied by nausea/vomiting and whether the headache was
238 accompanied by photophobia/phonophobia. These two variables have the greatest power in
239 distinguishing the two disorders. The PCC confirmed the strong correlation between elements of
240 the two lists. The odds ratios (ORs) for nausea/vomiting and photophobia/phonophobia were 0.4,
241 and were higher than those of the other headache-related variables. Through a simple correlation
242 analysis, we observe that patients with nausea/vomiting or photophobia/phonophobia were more
243 likely to be diagnosed with migraine headache than tension-type headache. To confirm and explore
244 the deeper relationship between the two disorders, we obtained the feature importance rankings
245 through the random forest model (Table 4). Among the variables, nausea/vomiting and
246 photophobia/phonophobia had importance values of 0.1897 and 0.1573, respectively, ranking
247 them as the top two variables.

248 In clinical practice, compared with patients with tension-type headaches, migraine patients have
249 more severe headaches and longer disease courses, and their headaches are usually accompanied
250 by nausea/vomiting and photophobia/phonophobia. In contrast, tension-type headaches are
251 generally mild, and not accompanied by nausea/vomiting and photophobia/phonophobia. Our
252 results are consistent with clinical experience. Therefore, we further compared the headache
253 severity and nausea/vomiting and photophobia/phonophobia between the two types of patients
254 (Fig 3). Compared with patients with tension-type headaches, migraine patients were more likely
255 to experience nausea/ vomiting and photophobia/phonophobia. Migraines were more severe and
256 were mainly distributed among the moderate to severe cases, while tension-type headaches were
257 mainly distributed among the mild to moderate cases.

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Table 3 chi-square test

Characteristic variable	P-value
Photophobia/phonophobia	P < 0.001
Nausea/vomiting	P < 0.001
Course	P < 0.001
Change after activities	P < 0.001
Severe intensity	P < 0.001
Alleviative way	P=0.00
Occiput	P=0.00
Throbbing	P=0.01
Spark	P=0.02

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Table 4 Random forest importance ranking

Characteristic variable	importance
Nausea/vomiting	0.1897
Photophobia/phonophobia	0.1573
Change after activities	0.1144
Course	0.1124
Severe intensity	0.1083
Alleviative way	0.0837
Occiput	0.0754
Spark	0.0604
Throbbing	0.0444

264

265 Discussion

266 Model building

267 AI is being applied to all types of fields, and its application to the medical field is a way for us to
 268 follow this trend. We used machine learning to identify primary headaches, which provided a
 269 starting point for advancing the transformation of AI. In this study, we established a discriminant
 270 model for the two types of primary headaches (migraine and tension-type headache) by machine
 271 learning algorithms based on 10 indicators. The diagnosis of primary headache, which is a
 272 functional disorder without an objective gold standard for diagnosis, is very difficult. Especially
 273 for the intermediate state of these two diseases, the ICHD-III diagnostic criteria are suitable for
 274 the diagnosis of only typical headache. For atypical headache and the intermediate headache state,
 275 many clinicians can rely only on their own clinical experience, and this subjective approach

276 inevitably has a great impact on the accuracy of disease diagnosis. In other words, clinical
277 diagnoses made by clinicians are highly subjective, varied and inconsistent. Furthermore, some
278 scholars believe that there may be overlap of multiple primary headaches, where multiple headache
279 symptoms exist simultaneously. Such overlapping headaches are common in cases of migraine
280 and tension-type headache. In addition, there are treatment differences among the different types
281 of headaches. Only clear diagnoses can improve these treatments. This intermediate headache state
282 and the overlapping conditions make it difficult for clinicians to accurately diagnose primary
283 headaches. Previous studies on primary headaches have been focused mainly on expert decision-
284 making systems based on international diagnostic standards [23-25]. However, it is difficult to
285 make a diagnosis based on the ICHD-III criteria for the intermediate state and the overlap of
286 clinical diseases. Perhaps it would be more efficient and effective to diagnose diseases through
287 individualized learning and reasoning based on samples than via a pure expert decision-making
288 system. Machine learning methods are an attractive option for such a task because they offer fast,
289 precise and intelligent analysis of multidimensional data. Therefore, in this study, we constructed
290 a model through different machine learning algorithms and explore the differences between
291 samples. In addition, for related headache data, it is possible to perform cluster analysis and
292 improve headache classification. Because of the subjective nature of the diagnosis, perform their
293 evaluations independently and reach different conclusions for the same case. After the promotion
294 and application of the decision-making system and through continuous learning and revision, the
295 diagnostic criteria used by clinicians can develop in the same direction.

296 **Feature selection**

297 To help clinicians quickly grasp the focus of the disease, the 10 variables were screened through
298 univariate statistical analysis and machine learning to identify the most important factors for

299 distinguishing migraines and tension-type headaches. The two most important factors were
300 nausea/vomiting and photophobia/phonophobia. They represent potential independent predictors.
301 In previous studies on simplified headache diagnostic criteria [26], a univariate migraine model
302 including nausea achieved a positive likelihood ratio of 4.8 and a negative likelihood ratio of 0.23.
303 By including the three variables for nausea, photophobia, and throbbing headache, the migraine
304 model achieved a positive likelihood ratio of 6.7 and a negative likelihood ratio of 0.23. The ID
305 Migraine™ screening instrument has been found to be an effective and reliable migraine screening
306 instrument, among the possible variables, disability, nausea, and photophobia provide the best
307 performance [27]. In our research, although we did not separately screen for nausea, vomiting,
308 photophobia, and phonophobia, the results we obtained through statistical analysis and machine
309 learning are generally consistent with those of previous studies. Nausea/vomiting,
310 photophobia/phonophobia, and phonophobia play a vital role in distinguishing migraines from
311 tension-type headaches.

312 Inevitably, our study has flaws. First, our discriminant model includes only the two types of
313 headaches with the highest incidence: migraine and tension-type headache. Although the model
314 can solve most of the problems related to the clinical diagnosis of headaches, other primary
315 headaches and secondary headaches are not included. Therefore, adding other headache categories
316 will be a future direction of expansion of our system. Second, the diagnosis of headache is strongly
317 affected by the clinical experience of the clinician. Although we followed up with each patient
318 after 2 weeks to assess headache improvement and verify the diagnosis, changes in the patient's
319 living habits or other factors might have impacted on the follow-up results. Third, we included
320 headache patients who visited a doctor, leading to selection bias. Patients with mild headaches

321 who did not seek medical attention from a doctor were not included in the study. Finally, our
322 sample size was small, we need to increase the sample size to verify and test the model.

323 **Conclusions**

324 Primary headache is a disorder with high incidence and low diagnostic accuracy. The goal of this
325 research is focused on the design and implementation of decision support system for diagnosing
326 primary headaches. This study used machine learning to construct a discriminant model for
327 migraines and tension-type headaches. The discriminant effect achieved by the integrated
328 algorithms, such as the random forest and gradient boosting algorithms, was better than that of a
329 single learner approaches, and the logistic regression model achieved the best discrimination
330 effect. Further research could be focused on creating new and more efficient tools and systems to
331 help and improve physicians' work and make diagnoses better. In addition, we identified the most
332 important factors for the identification of the two diseases through statistical analysis and machine
333 learning: nausea/vomiting and photophobia/phonophobia. These two factors represent potential
334 independent factors for identifying migraines and tension-type headaches, which can help
335 clinicians quickly grasp the focus of headaches.. However, our sample size was small, and we need
336 to increase the sample size to verify and improve the model.

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340 MY and M-GL collected the data, and contributed to the data management. F-FL conceived the
341 study, compared the results of the biostatistics feature rankings and the machine learning feature
342 rankings, wrote the manuscript. W-WA, G-SB, and F-JL helped design and revise the

343 questionnaire. G-SB revised the final version of the manuscript. All authors have read and
344 approved the final manuscript.

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- 428

Table 1 (on next page)

Patient baseline characteristics

1
2**Table 1** Patient baseline characteristics

Characteristics	Migraine (n=84)	Tension-type headache (n=89)	Total	P-value
Sex/n(%)	-	-	-	-
Female	20(23.8)	39(43.8)	59(34.1)	P=0.01
Male	64(76.2)	50(56.2)	114(65.9)	
Course/n(%)				
Year	11(13.1%)	38(42.7%)	49(28.3)	P < 0.001
Month	73(86.9%)	51(57.3%)	114(65.9)	
Throbbing/n(%)				
Yes	17(20.2)	6(6.7)	23(13.3)	P=0.01
No	67(79.8)	83(93.3)	150(86.7)	
Occiput/n(%)				
Yes	22(26.2)	43(48.3)	65(37.6)	P=0.00
No	62(73.8)	46(51.7)	108(62.4)	
Severe intensity/n(%)				
Light	13(15.5)	30(33.7)	43(24.9)	
Medium	44(52.4)	51(57.3)	95(54.9)	P < 0.001
Heavy	27(32.1)	8(9.0)	35(20.2)	
Nausea/ vomiting /n(%)				
Yes	44(52.4)	16(18.0)	60(34.7)	P < 0.001
No	40(47.6)	73(82.0)	113(65.3)	
Photophobia/ phonophobia /n(%)				
Yes	27(32.1)	4(4.5)	31(17.9)	P < 0.001
No	57(67.9)	85(95.5)	142(82.1)	
Spark/n(%)				
Yes	11(13.1)	3(3.4)	14(8.1)	P=0.02
No	73(86.9)	86(96.6)	159(91.9)	
Change after activities/n(%)				
Aggravate	41(48.8)	18(20.2)	59(34.1)	
Unchanged	38(45.2)	62(69.7)	100(57.8)	P < 0.001
Relieve	5(6.0)	9(10.1)	14(8.1)	
Alleviative methods/n(%)				
Persistence	9(10.7)	14(15.7)	23(13.3)	
Rest	25(29.8)	45(50.6)	70(40.5)	P=0.00
Drug	48(57.1)	25(28.1)	73(42.2)	
Else	2(2.4)	5(5.6)	7(4.0)	

Table 2 (on next page)

Evaluation of the discriminant effect of various models

1

Table 2 Evaluation of the discriminant effect of various models

	Accuracy	F1-score	ROC-AUC
Decision tree	0.72	0.68	0.72
Random Forests	0.80	0.79	0.85
Gradient boosting	0.79	0.79	0.82
Logistic regression	0.84	0.83	0.88
SVM-linear	0.82	0.81	0.82

2

Table 3 (on next page)

chi-square test

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Table 3 chi-square test

Characteristic variable	P-value
Photophobia/phonophobia	P < 0.001
Nausea/vomiting	P < 0.001
Course	P < 0.001
Change after activities	P < 0.001
Severe intensity	P < 0.001
Alleviative way	P=0.00
Occiput	P=0.00
Throbbing	P=0.01
Spark	P=0.02

3

Table 4 (on next page)

Random forest importance ranking

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Table 4 Random forest importance ranking

Characteristic variable	importance
Nausea/vomiting	0.1897
Photophobia/phonophobia	0.1573
Change after activities	0.1144
Course	0.1124
Severe intensity	0.1083
Alleviative way	0.0837
Occiput	0.0754
Spark	0.0604
Throbbing	0.0444

3

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Figure 1

Study flow chart

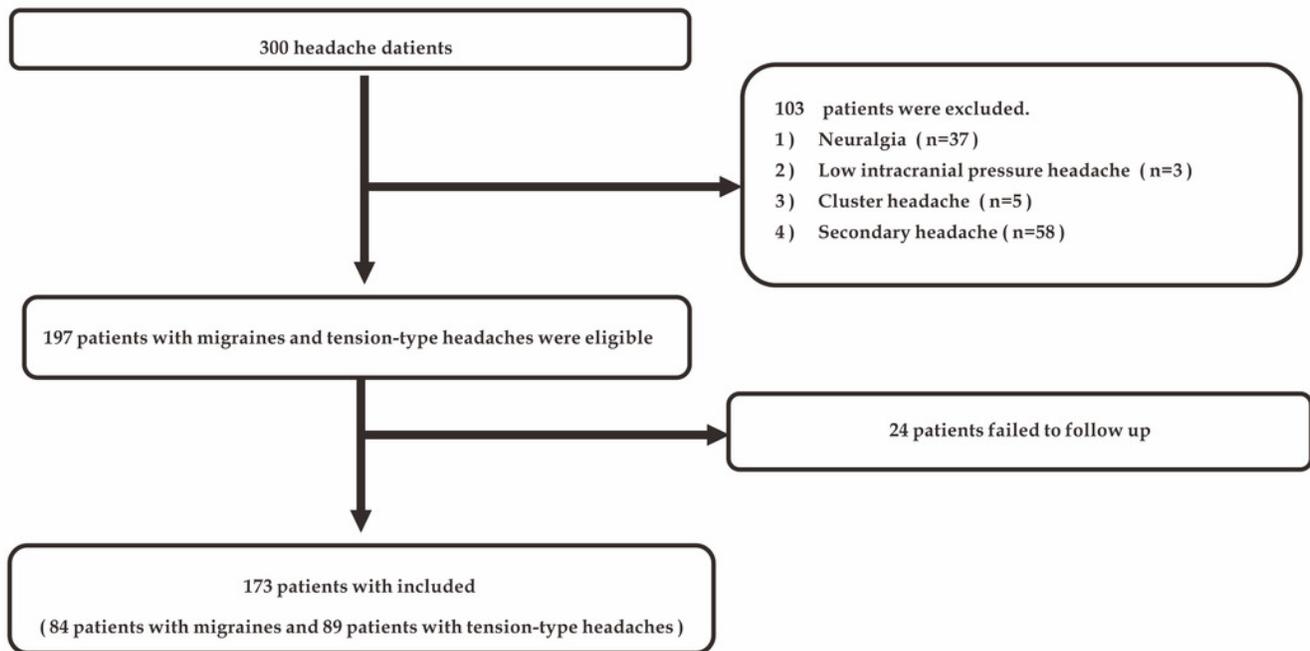


Figure 2

Pearson correlation coefficient

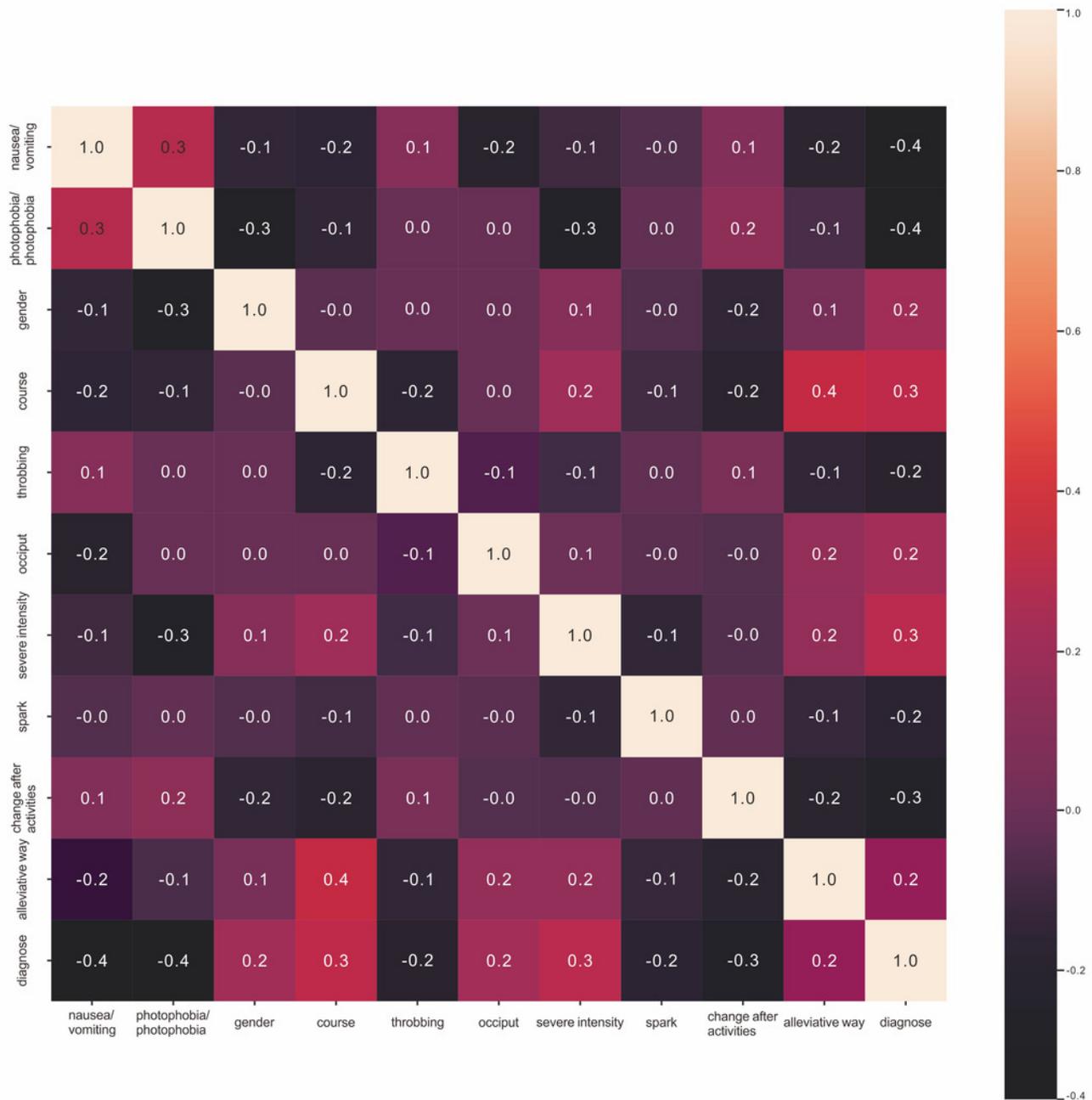


Figure 3

The correlation between headache severe intensity, nausea/vomiting, and photophobia/phonophobia

