

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 low diagnostic accuracy; the incidence of migraine and tension-type headache ranks first among primary headaches. Artificial intelligence (AI) decision support systems have shown great potential in the medical field. Therefore, we attempt to use machine learning to build a clinical decision-making system for primary headaches. **Methods** □ The demographic data and headache characteristics of 173 patients were collected by questionnaires. Decision tree, random forest, gradient boosting algorithm and support vector machine (SVM) models were used to construct a discriminant model and a confusion matrix was used to calculate the 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 has the best discrimination effect, with the accuracy reaching 0.84 and the area under the ROC curve also being the largest at 0.90. 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 □ with the accuracy reaching 0.74 and the area under the ROC curve being at 0.74. **Conclusions** □ Applying machine learning to the decision-making system for primary headaches can achieve a high diagnostic accuracy. Among them, the discrimination effect obtained by the integrated algorithm is significantly better than that of a single learner. Second, nausea/vomiting, photophobia/phonophobia may be the most important factors for distinguishing migraine from tension-type headaches.

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A decision support system for primary headache

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11 Abstract

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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 0.90. 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 with the accuracy reaching 0.74 and the area under the ROC curve being at 0.74. **Conclusions**
29 : Applying machine learning to the decision-making system for primary headaches can achieve
30 a high diagnostic accuracy. Among them, the discrimination effect obtained by the integrated
31 algorithm is significantly better than that of a single learner. Second, nausea/vomiting,
32 photophobia/phonophobia may be the most important factors for distinguishing migraine from
33 tension-type headaches.

34 Introduction

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

44 Headaches are divided into primary headaches and secondary headaches. There are many causes
45 of headaches. Due to the similarity of symptoms, it is easy for general practitioners to miss or
46 misdiagnose the type of headache. Furthermore, the International Headache Society (IHS) released
47 the latest headache classification in January 2018, which is the International Classification of
48 Headache Disorders (ICHD-III) [7], which lists more than 200 headache variants. This

49 complicated classification creates a very challenging task for general clinicians. There is no
50 objective gold standard, which contributes to the difficulty of diagnosing and classifying
51 headaches. In addition, because the medical community has generally not paid enough attention to
52 headaches in clinical practice for a long time, the proficiency level of clinicians regarding the
53 headache classification is uneven. For example, "vascular headache" and "nervous headache" are
54 still used to diagnose primary headache.

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

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

71 differences in the treatment of the two disorders, misdiagnosis and missed diagnosis inevitably
72 delay the appropriate treatment of the patients[9].

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

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

94 in terms of the sensitivity and specificity of this system for diagnosing headaches [20].
95 Considering the incomplete language rules when human experts express their knowledge,
96 Monire et al improved the algorithm and used the Learning-From-Examples (LEF) algorithm to
97 train the diagnostic fuzzy system, and the correct recognition rate reached 85%. They further
98 proposed SVM- and multilayer perceptron (MLP)--based decision support systems, which
99 achieved accuracy rates of 90% and 88%, respectively [21]. Simi'c et al create a hybrid
100 intelligent system for diagnosing primary headache disorders, applying various mathematical,
101 statistical and artificial intelligence techniques[22]. Although various types of research have been
102 devoted to computer decision support systems, there are still major obstacles to their widespread
103 use in clinical practice. Machine learning applied to medical records can be an effective tool to
104 predict disease. In China, machine learning methods for diagnosing primary headache remain
105 lacking.
106 Therefore, to achieve a higher headache diagnostic accuracy, we collected information from
107 primary headache patients in neurology clinics through questionnaires and then entered the data
108 into the system. We compared various machine learning algorithms to identify the best model.
109 Furthermore, through feature selection, we identified the most important factors for distinguishing
110 migraines from tension-type headaches, which provide a basis for clinicians to quickly diagnose
111 headaches.

112 **Materials & Methods**

113 This is a cross-sectional study designed to obtain a diagnostic discriminant model for migraines
114 and tension-type headaches and to screen out the most important factors for distinguishing the two.
115 The study was approved by the Ethics Committee of the Ninth People's Hospital affiliated to
116 Shanghai Jiao Tong University Medicine (approval no.SH9H-2021-T72-1), and met the

117 requirements of the Declaration of Helsinki. Eligible patients were patients diagnosed with
118 headaches between October 2019 and September 2020 at the Department of Neurology, Shanghai
119 Ninth People's Hospital. All the patients were residents of China. Before the study, we obtained
120 signed informed consent from the participating patients. Two weeks after a patient's questionnaire
121 was collected, we followed up on the patient's headache improvement to further verify the
122 diagnosis. Finally, we included 173 patients with a definite diagnosis of primary headache (84
123 patients with migraine headaches and 89 patients with tension-type headaches) for research.

124 **Data acquisition**

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

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

140 symptoms. Therefore, we performed a binary classification of the collected data and obtained a
141 total of 48 variables. Considering that the incidence of many variables was extremely low, we first
142 identified 10 variables with statistically significant differences between migraines and tension-
143 type headaches. After data transformation and data reduction, the data sheet used to acquire data
144 during the clinical interview is shown in Table 1.

145 **Discriminant model establishment**

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

151 Decision tree

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

157 Random forest

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

163 SVM

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

170 Gradient boosting

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

175 Logistic regression

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

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

184
$$F1\ score = \frac{2Precision * Recall}{Precision + Recall}$$

185 **Feature selection**

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

208 **Results**

209 **Patient baseline characteristics**

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

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. After the **CROSS-**
220 **validation**, the mean accuracy, F1 score were calculated through the confusion matrix (Table 2),
221 the discrimination result curve (ROC curve) was constructed, and the area under the ROC curve
222 were measured. The mean accuracy of the decision tree is 0.72, which was significantly lower
223 than that of the integrated learning algorithm and SVM models. The random forest, gradient
224 boosting algorithm, and SVM models have similar discrimination effects; their mean accuracy
225 scores were 0.80, 0.79, and 0.82, and the mean areas under the ROC curves were 0.85, 0.82, and
226 0.82, respectively and the mean F1 score were 0.79, 0.79, and 0.81, respectively. Logistic
227 regression had the best discrimination effect, with the mean accuracy reaching 0.84 and the mean
228 area under the ROC curve also being the largest among the methods, at 0.90. The discrimination
229 effect achieved by the integrated algorithm was better than that of a single learner method, and
230 among the models, logistic regression achieved the best discrimination effect.

231 **Feature selection**

232 For feature selection, we applied two methods: univariate statistical analysis and machine learning.
233 For the univariate test, we used the PCC (Fig 2) and the chi-square test (Table 3) to compare each
234 feature between the two groups and rank them according to p-value. Through the univariate chi-
235 square tests, we determined that the smallest p-values were obtained for the variables indicating
236 whether the headache was accompanied by nausea/vomiting and whether the headache was
237 accompanied by photophobia/phonophobia. These two variables have the greatest power in
238 distinguishing the two disorders. The PCC confirmed the strong correlation between elements of
239 the two lists. The odds ratios (ORs) for nausea/vomiting and photophobia/phonophobia were 0.4,
240 and were higher than those of the other headache-related variables. Through a simple correlation
241 analysis, we observe that patients with nausea/vomiting or photophobia/phonophobia were more
242 likely to be diagnosed with migraine headache than tension-type headache. To confirm and explore
243 the deeper relationship between the two disorders, we obtained the feature importance rankings
244 through the random forest model (Table 4). Among the variables, nausea/vomiting and
245 photophobia/phonophobia had importance values of 0.1897 and 0.1573, respectively, ranking
246 them as the top two variables. To verify the predictive power of nausea/vomiting and
247 photophobia/phonophobia, we trained the logistic regression on these two features, with the mean
248 accuracy reaching 0.74 and the mean area under the ROC curve reaching 0.74 (Table 5).

249 In clinical practice, compared with patients with tension-type headaches, migraine patients have
250 more severe headaches and longer disease courses, and their headaches are usually accompanied
251 by nausea/vomiting and photophobia/phonophobia. In contrast, tension-type headaches are
252 generally mild, and not accompanied by nausea/vomiting and photophobia/phonophobia. Our
253 results are consistent with clinical experience. Therefore, we further compared the headache
254 severity and nausea/vomiting and photophobia/phonophobia between the two types of patients

255 (Fig 3). Compared with patients with tension-type headaches, migraine patients were more likely
256 to experience nausea/ vomiting and photophobia/phonophobia. Migraines were more severe and
257 were mainly distributed among the moderate to severe cases, while tension-type headaches were
258 mainly distributed among the mild to moderate cases.

259 **Discussion**

260 **Model building**

261 AI is being applied to all types of fields, and its application to the medical field is a way for us to
262 follow this trend. We used machine learning to identify primary headaches, which provided a
263 starting point for advancing the transformation of AI. In this study, we established a discriminant
264 model for the two types of primary headaches (migraine and tension-type headache) by machine
265 learning algorithms based on 10 indicators. The diagnosis of primary headache, which is a
266 functional disorder without an objective gold standard for diagnosis, is very difficult. Especially
267 for the intermediate state of these two diseases, the ICHD-III diagnostic criteria are suitable for
268 the diagnosis of only typical headache. For atypical headache and the intermediate headache state,
269 many clinicians can rely only on their own clinical experience, and this subjective approach
270 inevitably has a great impact on the accuracy of disease diagnosis. In other words, clinical
271 diagnoses made by clinicians are highly subjective, varied and inconsistent. Furthermore, some
272 scholars believe that there may be overlap of multiple primary headaches, where multiple headache
273 symptoms exist simultaneously. Such overlapping headaches are common in cases of migraine
274 and tension-type headache. In addition, there are treatment differences among the different types
275 of headaches. Only clear diagnoses can improve these treatments. This intermediate headache state
276 and the overlapping conditions make it difficult for clinicians to accurately diagnose primary
277 headaches. Previous studies on primary headaches have been focused mainly on expert decision-

278 making systems based on international diagnostic standards [23-25]. However, it is difficult to
279 make a diagnosis based on the ICHD-III criteria for the intermediate state and the overlap of
280 clinical diseases. Perhaps it would be more efficient and effective to diagnose diseases through
281 individualized learning and reasoning based on samples than via a pure expert decision-making
282 system. Machine learning methods are an attractive option for such a task because they offer fast,
283 precise and intelligent analysis of multidimensional data. Therefore, in this study, we constructed
284 a model through different machine learning algorithms and explore the differences between
285 samples. In addition, for related headache data, it is possible to perform cluster analysis and
286 improve headache classification. Because of the subjective nature of the diagnosis, perform their
287 evaluations independently and reach different conclusions for the same case. After the promotion
288 and application of the decision-making system and through continuous learning and revision, the
289 diagnostic criteria used by clinicians can develop in the same direction.

290 **Feature selection**

291 To help clinicians quickly grasp the focus of the disease, the 10 variables were screened through
292 univariate statistical analysis and machine learning to identify the most important factors for
293 distinguishing migraines and tension-type headaches. The two most important factors were
294 nausea/vomiting and photophobia/phonophobia. They represent potential independent predictors.
295 In previous studies on simplified headache diagnostic criteria [26], a univariate migraine model
296 including nausea achieved a positive likelihood ratio of 4.8 and a negative likelihood ratio of 0.23.
297 By including the three variables for nausea, photophobia, and throbbing headache, the migraine
298 model achieved a positive likelihood ratio of 6.7 and a negative likelihood ratio of 0.23. The ID
299 Migraine™ screening instrument has been found to be an effective and reliable migraine screening
300 instrument, among the possible variables, disability, nausea, and photophobia provide the best

301 performance [27]. In our research, although we did not separately screen for nausea, vomiting,
302 photophobia, and phonophobia, the results we obtained through statistical analysis and machine
303 learning are generally consistent with those of previous studies. To ensure the integrity of the
304 experiment, we trained the logistic regression based on these two features. According to the results,
305 the multi-features model is better than the two-features model. However, the two features selected
306 can help clinicians grasp the focus of the disease as soon as possible. Nausea/vomiting,
307 photophobia/phonophobia, and phonophobia play a vital role in distinguishing migraines from
308 tension-type headaches.

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

320 **Conclusions**

321 Primary headache is a disorder with high incidence and low diagnostic accuracy. The goal of this
322 research is focused on the design and implementation of decision support system for diagnosing
323 primary headaches. This study used machine learning to construct a discriminant model for
324 migraines and tension-type headaches. The discriminant effect achieved by the integrated

325 algorithms, such as the random forest and gradient boosting algorithms, was better than that of a
326 single learner approaches, and the logistic regression model achieved the best discrimination
327 effect. Further research could be focused on creating new and more efficient tools and systems to
328 help and improve physicians' work and make diagnoses better. In addition, we identified the most
329 important factors for the identification of the two diseases through statistical analysis and machine
330 learning: nausea/vomiting and photophobia/phonophobia. These two factors represent potential
331 independent factors for identifying migraines and tension-type headaches, which can help
332 clinicians quickly grasp the focus of headaches. However, our sample size was small, and we
333 need to increase the sample size to verify and improve the model.

334 **Acknowledgements**

335 Funding from the Jinhua Science and Technology Bureau (No.2020-3-036) and the project of the
336 Shanghai Science and Technology Commission (14411972200) are gratefully acknowledged. X-
337 MY and M-GL collected the data, and contributed to the data management. F-FL conceived the
338 study, compared the results of the biostatistics feature rankings and the machine learning feature
339 rankings, wrote the manuscript. W-WA, G-SB, and F-JL helped design and revise the
340 questionnaire. G-SB revised the final version of the manuscript. All authors have read and
341 approved the final manuscript.

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345 **References**

- 346 [1] K. Hagen, A. N. Åsberg, B. L. Uhlig, E. Tronvik, E. Brenner, M. Stjern, G. Helde, G. B.
347 Gravdahl and T. Sand. 2018. The epidemiology of headache disorders: a face-to-face interview of
348 participants in HUNT4. *J Headache Pain* 19:25. 10.1186/s10194-018-0854-2
349 [2] S. Yu, R. Liu, G. Zhao, X. Yang, X. Qiao, J. Feng, Y. Fang, X. Cao, M. He and T. Steiner.
350 2012. The prevalence and burden of primary headaches in China: a population-based door-to-door
351 survey. *Headache* 52:582-591. 10.1111/j.1526-4610.2011.02061.x

- 352 [3] C. Yao, Y. Wang, L. Wang, Y. Liu, J. Liu, J. Qi, Y. Lin, P. Yin and M. Zhou. 2019. Burden of
353 headache disorders in China, 1990-2017: findings from the Global Burden of Disease Study 2017.
354 *J Headache Pain* 20:102. 10.1186/s10194-019-1048-2
- 355 [4] T. Takeshima, Q. Wan, Y. Zhang, M. Komori, S. Stretton, N. Rajan, T. Treuer and K. Ueda.
356 2019. Prevalence, burden, and clinical management of migraine in China, Japan, and South Korea:
357 a comprehensive review of the literature. *J Headache Pain* 20:111. 10.1186/s10194-019-1062-4
- 358 [5] D. Saylor and T. J. Steiner. 2018. The Global Burden of Headache. *Semin Neurol* 38:182-190.
359 10.1055/s-0038-1646946
- 360 [6] K. Malmberg-Ceder, M. Haanpää, P. E. Korhonen, H. Kautiainen, V. Veromaa and S. Soinila.
361 2019. The role of psychosocial risk factors in the burden of headache. *J Pain Res* 12:1733-1741.
362 10.2147/jpr.S165263
- 363 [7] 2018. Headache Classification Committee of the International Headache Society (IHS) The
364 International Classification of Headache Disorders, 3rd edition. *Cephalalgia* 38:1-211.
365 10.1177/0333102417738202
- 366 [8] Á. L. G. MD, E. R. MD, S. H. MD, M. J. N. NP, L. B. NP, M. L. P. MD, E. C. MD, P. M. MD,
367 R. F. MD and PhD. 2011. Characteristics of the First 1000 Headaches in an Outpatient Headache
368 Clinic Registry. *Headache: The Journal of Head and Face Pain* 51.
- 369 [9] J. K. Porter, G. L. Di Tanna, R. B. Lipton, S. Sapura and G. Villa. 2019. Costs of Acute Headache
370 Medication Use and Productivity Losses Among Patients with Migraine: Insights from Three
371 Randomized Controlled Trials. *Pharmacoecon Open* 3:411-417. 10.1007/s41669-018-0105-0
- 372 [10] C. Krittanawong, H. U. H. Virk, S. Bangalore, Z. Wang, K. W. Johnson, R. Pinotti, H. Zhang,
373 S. Kaplin, B. Narasimhan, T. Kitai, U. Baber, J. L. Halperin and W. H. W. Tang. 2020. Machine
374 learning prediction in cardiovascular diseases: a meta-analysis. *Sci Rep* 10:16057.
375 10.1038/s41598-020-72685-1
- 376 [11] M. W. Huang, C. W. Chen, W. C. Lin, S. W. Ke and C. F. Tsai. 2017. SVM and SVM
377 Ensembles in Breast Cancer Prediction. *PLoS One* 12:e0161501. 10.1371/journal.pone.0161501
- 378 [12] J. Li, Z. Weng, H. Xu, Z. Zhang, H. Miao, W. Chen, Z. Liu, X. Zhang, M. Wang, X. Xu and
379 Q. Ye. 2018. Support Vector Machines (SVM) classification of prostate cancer Gleason score in
380 central gland using multiparametric magnetic resonance images: A cross-validated study. *Eur J*
381 *Radiol* 98:61-67. 10.1016/j.ejrad.2017.11.001
- 382 [13] T. Shen, J. Jiang, Y. Li, P. Wu, C. Zuo and Z. Yan. 2018. Decision Supporting Model for
383 One-year Conversion Probability from MCI to AD using CNN and SVM. *Annu Int Conf IEEE*
384 *Eng Med Biol Soc* 2018:738-741. 10.1109/EMBC.2018.8512398
- 385 [14] B. Abbasi and D. M. Goldenholz. 2019. Machine learning applications in epilepsy. *Epilepsia*
386 60:2037-2047. 10.1111/epi.16333
- 387 [15] M. Kocher, M. I. Ruge, N. Galldiks and P. Lohmann. 2020. Applications of radiomics and
388 machine learning for radiotherapy of malignant brain tumors. *Strahlenther Onkol* 196:856-867.
389 10.1007/s00066-020-01626-8
- 390 [16] J. T. Senders, O. Arnaut, A. V. Karhade, H. H. Dasenbrock, W. B. Gormley, M. L. Broekman
391 and T. R. Smith. 2018. Natural and Artificial Intelligence in Neurosurgery: A Systematic Review.
392 *Neurosurgery* 83:181-192. 10.1093/neuros/nyx384
- 393 [17] S. H. Chae, Y. Kim, K. S. Lee and H. S. Park. 2020. Development and Clinical Evaluation of
394 a Web-Based Upper Limb Home Rehabilitation System Using a Smartwatch and Machine
395 Learning Model for Chronic Stroke Survivors: Prospective Comparative Study. *JMIR Mhealth*
396 *Uhealth* 8:e17216. 10.2196/17216
- 397 [18] B. Krawczyk, D. Simić, S. Simić and M. Woźniak. 2013. Automatic diagnosis of primary

398 headaches by machine learning methods. *Open Medicine* 8:157-165. 10.2478/s11536-012-0098-5
399 [19] G. Vandewiele, F. De Backere, K. Lannoye, M. Vanden Berghe, O. Janssens, S. Van Hoecke,
400 V. Keereman, K. Paemeleire, F. Ongenae and F. De Turck. 2018. A decision support system to
401 follow up and diagnose primary headache patients using semantically enriched data. *BMC Med*
402 *Inform Decis Mak* 18:98. 10.1186/s12911-018-0679-6
403 [20] Y. Z. D. Z. K. Xiangyong. 2019. Assistant decision-making system based on international
404 diagnostic criteria for primary headache disorders. *Application Research of Computers* 36:2.
405 [21] M. Khayamnia, M. Yazdchi, A. Heidari and M. Foroughipour. 2019. Diagnosis of Common
406 Headaches Using Hybrid Expert-Based Systems. *J Med Signals Sens* 9:174-180.
407 10.4103/jmss.JMSS_47_18
408 [22] S. Simić, J. R. Villar, J. L. Calvo-Rolle, S. R. Sekulić, S. D. Simić and D. Simić. 2021. An
409 Application of a Hybrid Intelligent System for Diagnosing Primary Headaches. *Int J Environ Res*
410 *Public Health* 18. 10.3390/ijerph18041890
411 [23] R. Costabile, G. Catalano, B. Cuteri, M. C. Morelli, N. Leone and M. Manna. 2020. A logic-
412 based decision support system for the diagnosis of headache disorders according to the ICHD-3
413 international classification.
414 [24] A. Roesch, M. A. Dahlem, L. Neeb and T. Kurth. 2020. Validation of an algorithm for
415 automated classification of migraine and tension-type headache attacks in an electronic headache
416 diary. *J Headache Pain* 21:75. 10.1186/s10194-020-01139-w
417 [25] L. Hui, H. C. Keh, C. C. Meng and Z. Y. Liu. 2018. Clinical Application of Decision Support
418 System for Treatment of Migraine. *International Conference on Frontier Computing*.
419 [26] V. T. Martin, D. B. Penzien, T. T. Houle, M. E. Andrew and K. R. Lofland. 2005. The
420 predictive value of abbreviated migraine diagnostic criteria. *Headache* 45:1102-1112.
421 10.1111/j.1526-4610.2005.00234.x
422 [27] R. B. Lipton, D. Dodick, R. Sadovsky, K. Kolodner, J. Endicott, J. Hettiarachchi and W.
423 Harrison. 2003. A self-administered screener for migraine in primary care: The ID Migraine
424 validation study. *Neurology* 61:375-382. 10.1212/01.wnl.0000078940.53438.83
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Table 1 (on next page)

Patient baseline characteristics

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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

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3**Table 2** Evaluation of the discriminant effect of various models

	80:20			70:30			60:40			Mean		
	Accuracy	F1	AUC									
Decision tree	0.74	0.69	0.74	0.74	0.65	0.64	0.64	0.69	0.78	0.72	0.68	0.72
Random Forests	0.89	0.86	0.90	0.90	0.78	0.79	0.79	0.74	0.85	0.80	0.79	0.85
Gradient boosting	0.89	0.87	0.91	0.91	0.71	0.70	0.70	0.79	0.86	0.79	0.79	0.82
Logistic regression	0.91	0.90	0.95	0.95	0.82	0.88	0.88	0.77	0.87	0.84	0.83	0.90
SVM-linear	0.89	0.87	0.84	0.84	0.81	0.82	0.82	0.75	0.81	0.82	0.81	0.82

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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

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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

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Table 5 (on next page)

Evaluation of the predictive power of the two selected features.

Table 5 Evaluation of the predictive power of the two selected features.

Logistic regression	Accuracy	F1-score	ROC-AUC
80:20	0.74	0.61	0.71
70:30	0.71	0.69	0.73
60:40	0.76	0.74	0.78
Mean	0.74	0.68	0.74

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Figure 1

Study flow chart

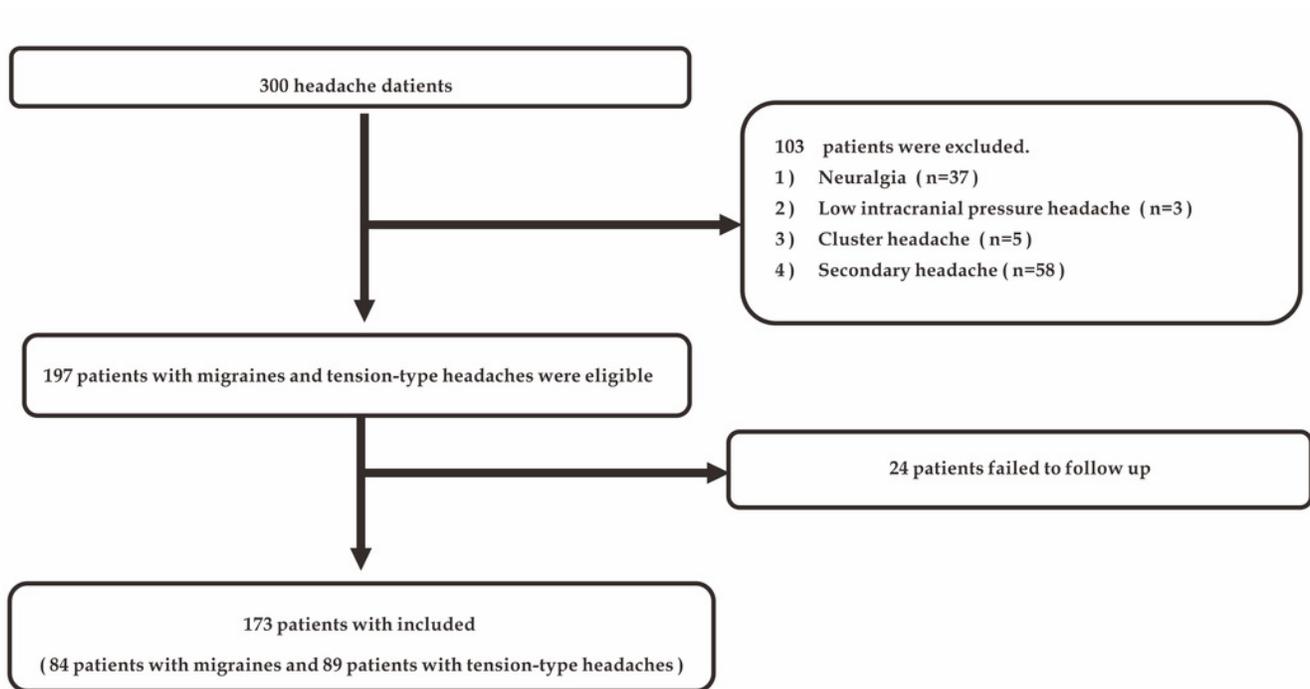


Figure 2

Pearson correlation coefficient

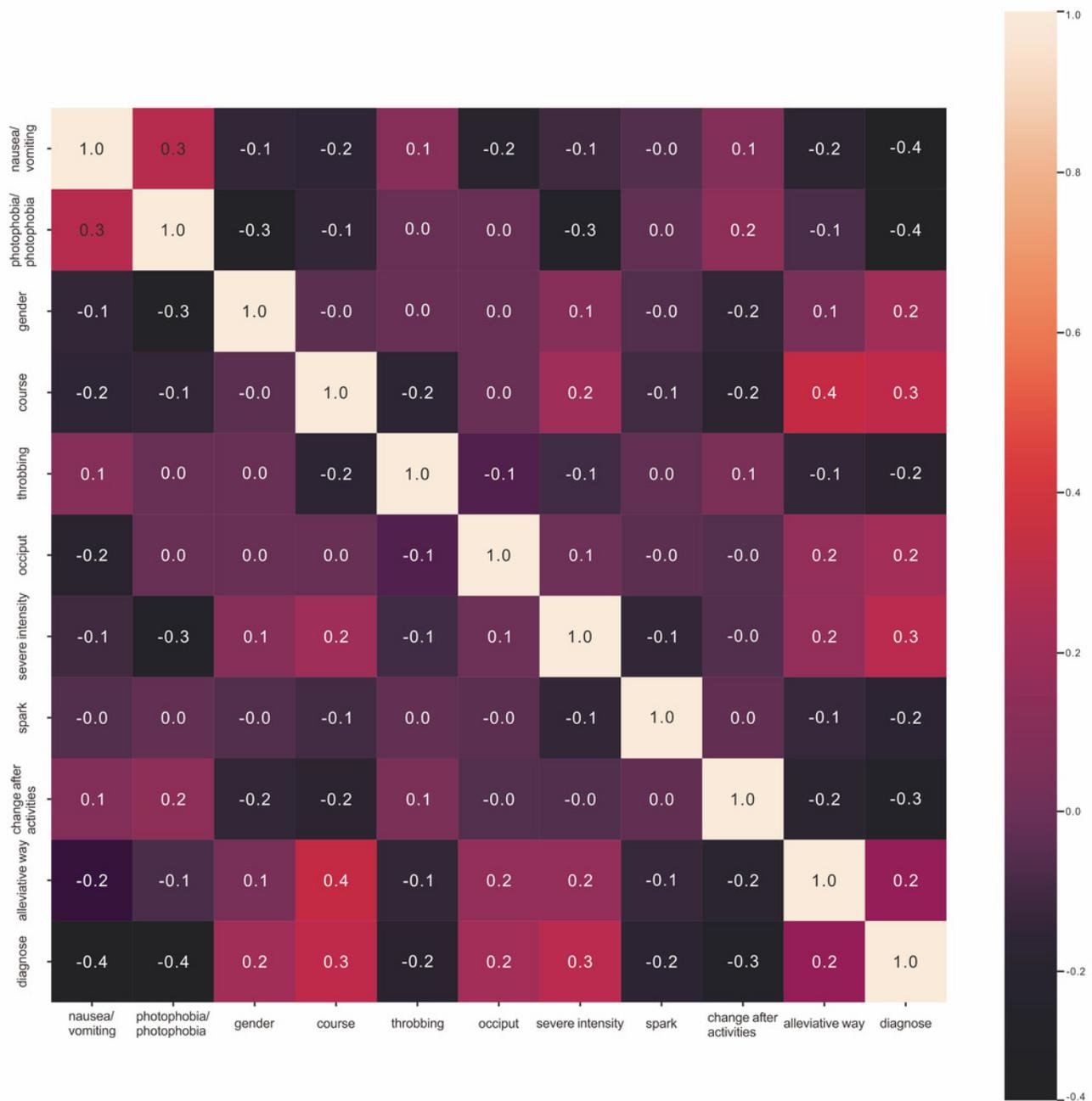


Figure 3

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

