AR-ANN: Incorporating Association Rule Mining in Artificial Neural Network for Thyroid Disease Knowledge Discovery and Diagnosis

Dongyang Li, Dan Yang, Jing Zhang, Xuedong Zhang

***Abstract*—Thyroid disease is a common high-incidence disease in the field of endocrine. Mastering the disease influence factors plays a vital role in the successful diagnosis of the disease. In this paper, we propose a thyroid disease knowledge discovery and diagnosis framework AR-ANN, which integrates association rule mining and artificial neural network. Two rule generation algorithms (Apriori and Predictive Apriori) are used to investigate the sick and healthy factors which contribute to thyroid disease. These algorithms are also used to select the most frequent features and to reduce the dimensions. After that, we use one of the most classical artificial neural networks, i.e. BP neural network, to diagnose thyroid disease. We use SPSS Statistics to convert the numerical data into nominal data in preprocessing. Analyzing the Top-7 association rules generated by the two algorithms, we know that age and sex are the two most important factors. Thyroid disease have different effects on people of different age intervals, and the elderly from 60 to 90 are the most likely to suffer from thyroid disease. The results also show that 50 to 60 years old is the age interval with the highest recurrence rate of thyroid disease. For gender factor, men have more chance of being free from thyroid disease than women. Thyroid disease knowledge from these rules is used as the attribute input of BP neural network for diagnosing thyroid disease. Two real world thyroid datasets in UCI machine learning repository are applied. The experimental results show that the performance of AR-ANN is better, which also shows the feasibility and practical value of association rule mining algorithm and BP neural network in thyroid disease assistant diagnosis.**

***Index Terms*—Association rule mining; thyroid disease; BP neural network**

I. INTRODUCTION

Thyroid disease is a high incidence of disease inendocrine disease. On September 08, 2010, the Endocrine Branch of the Chinese Medical Association announces that thyroid disease has become the second largest disease inendocrine disease besides diabetesmellitus [1], and there are many people, who are about 30% of young (0-44) and middle-aged people (45-59) and more than 50% of the elderly (60-90) [2], associated with thyroid disease each year [3]. With such a high incidence of thyroid diseases, it is necessary to gain a clearer understanding of the risk factors for thyroid diseases, as well as improve accuracy of diagnosis. According to the latest research by Taylor et al. [4], the main causes of thyroid disease may be: gender, insufficient iodine intake, excessive iodine intake, the transition from iodine deficiency to adequate iodine intake, other autoimmune conditions, genetic risk factors, smoking, alcohol consumption, drug abuse, selenium deficiency, infection and syndrome.

Association rule mining, one of the data mining technologies, is currently applied to discover the relationships between different patient attributes in medical big data [5]. And the World Health Organization has found that data mining algorithm can greatly improve some problems in the medical field. In WHO research, the emphasis is placed on the medical data repository, which can contribute to 1) medical diagnosis and prediction 2) patient health planning 3) monitoring and evaluation of health care systems 4) hospital and health service management and disease prevention [6]. So, this paper presents rule extraction experiments on thyroid disease using two association rule mining algorithms – Apriori and Predictive Apriori.

In recent years, artificial neural network can not only process text information [7-10], but also extract image information. So it has been widely used in disease diagnosis [5]. BP neural network is the most widely used neural network at present. We combine association rule mining algorithm and BP neural network to form a new diagnosis framework (AR-ANN), which is also the software core of computer aided diagnosis system. Experts have always emphasized the importance of computer-aided diagnosis. This system not only improves the consistency of diagnosis and the success rate of treatment, but also reduces the time and the cost of diagnosis [11].

II. RELATED WORK

In recent years, there are an increasing number of studies that use association rule mining algorithms to mine medical big data, and apply artificial neural networks to diagnose disease. We have a brief literature review in terms of thyroid

Dongyang Li, is with School of Computer Science and Software Engineering, University of Science and Technology LiaoNing, Anshan, China (e-mail: hclidonyang@ 163.com)

Dan Yang, the corresponding author, is associate professor with School of Computer Science and Software Engineering, University of Science and Technology LiaoNing, Anshan, China (e-mail: asyangdan@ 163.com)

Jing Zhang, is with School of Computer Science and Software Engineering, University of Science and Technology LiaoNing, Anshan, China (e-mail: zwinerj@ 163.com)

Xuedong Zhang, is with School of Computer Science and Software Engineering, University of Science and Technology LiaoNing, Anshan, China (e-mail: zhangxuedong@ustl.edu.com)

disease, association rule mining algorithms (i.e. Apriori algorithm and Predictive Apriori algorithm), and neural network in the field of medical big data.

In the field of thyroid disease, Ming Zhan et al. [12] conducted a genome-wide association study of TSH levels in 1346 Chinese Han individuals. Experimental results had shown that sex hormones affected the activity of deiodinase in liver and kidney tissues, and enzyme affect the secretion of thyroxine, but as the age increases, the effect would gradually disappear. In [13], Kaloumenou et al. assessed thyroid function in children and adolescents in an iodinereplete area to explore possible effects of age, gender, puberty and adiposity by Thyrotropin (TSH), total triiodothyronine (T3), total thyroxine (T4), free thyroxine (FT4) and the T4/T3 ratio. They concluded that estrogens might exert a suppressive effect on the pituitary-thyroid axis after puberty. TSH values were not correlated with BMISDS, whereas T4/T3 ratio in boys and FT4 in girls were negatively correlated with BMI-SDS. In [14], Bauer et al. found that subclinical hypothyroidism had a higher incidence in women, which was found to occur in up to 20% of postmenopausal women. And disturbances of thyroid system function, which occurred commonly in females, might complicate the diagnosis and treatment of mood disorders. In particular, this was clinically relevant during lithium treatment because lithium might impair vital thyroid metabolic pathways secondary to its anti-thyroid activity. In [15], Wang Mingxue et al. found that age and gender could affect the thyroxine levels of healthy people in various regions. Therefore, it was innovative and important for the laboratory to test by age and gender.

Association rule mining algorithms had widely applied in medical knowledge extraction. Xiong Juan et al. [16] proposed an improved association rule mining algorithm, and they took hand-foot-mouth disease in Wuhan as an example to compare the application value of different statistical methods in the seasonal study of hand-foot mouth disease. They also provided scientific basis for seasonal prevention and the control of hand-foot-mouth disease. Anindita et al. [17] proposed an efficient association rule mining algorithm to identify the symptoms and risk factors for three adverse diseases: cardiovascular disease, hepatitis and breast cancer. According to the international classification of disease, 10th revision (ICD-10) diagnosis system from NHID from 2011 to 2013 in youths aged 18 or younger, Kim et al. [18] applied Apriori algorithm to categorize mental disorder. And the most interesting rule had been mined, mood/affective disorder was the most prevalent comorbid psychiatric disorder of ADHD youths. The paper also proved the practicality of association rule mining to discover the comorbidity of ADHD in large amount real-data such as the Korean NHID was mostly confirmed by past studies. The work proposed by Jungtae et al. [19] used association rule mining to identify frequently combined two-herb and three-herb sets and they used network analysis to divide the herbs into several modules according to prescription pattern. They found that the most frequently used two-herb combination in alopecia treatment consisted of Polygonum multiflorum Thunb and Angelica sinensis Dlels. And the most frequently used three-herb combination was Polygonum multiflorum Thunb, Angelica sinensis Dlels and Ligusticum chuanxiong Hort. In the work [20], Yang Huisheng et al. used association rules to analyze Fufangkushen injection in combination with other modern medications in treating lung cancer based on the electrical medical records in real world clinical situations and used Apriori algorithm to analyze the specific association rule in combined drug use. In that work, the distribution characteristics in combined application and association combinations of Fufangkushen injection had specific rules, consistent with the clinical orientation of this drug in treatment of lung cancer. Among association rule mining algorithms, Apriori algorithm is widely used in medical database. Zhang Yinghui et al. [21] used Apriori algorithm to extract the rules of Fufangkushen injection in combination with other modern medications while treating malignant esophageal tumors. They found that detailed correlations between modern medications applying accompany with Fufangkushen injection factors were revealed based on Apriori algorithm, which were generally correspond to clinical guidelines and contributed to reasonable application of Fufangkushen injection in clinical treatment. Apriori algorithm was used to analyze the cause, disease, pathogenesis and their relations of Professor Yao Meiling's asthma diagnosis and treatment by Chen Cong et al. [22]. Their research had the conclusion that the asthma attack was mainly in the form of the exterior and interior taiyin lung channel of hand and the syndrome type was mainly sputum and fluid. There were 7 types of syndromes including rheumatism, depression of taiyin lung channel of hand etc. Except Apriori algorithm, there were other classical algorithms. In the work [23], three association rule mining algorithms (Apriori, Predictive Apriori and Tertius) were applied by Naharet al. to discover most of the significant prevention factors against these specific types of cancer (bladder, breast, cervical, lung, prostate and skin cancer). They found Apriori was the most useful association rule mining algorithm to be used in the discovery of prevention factors. In the work [24], Nahar et al. applied the same three association rule mining algorithms to detect factors which contribute to heart disease. According to the association rule mining algorithms on sick and healthy individuals, they found males were seen to have more chance of coronary heart disease than females. Delgado et al. [25] used four association rule mining algorithms (Apriori, FP-Growth, Predictive Apriori, Tertius) and three machine learning algorithms to analyze the possible causes of the reduction of autopsies.

Neural network has been widely used in different fields. In the field of climate, related work [26] applied artificial neural network in forecasting the seasonal rainfall. Related work [27] predicted story drift of building by BP neural network. In financial field, neural network was used to predict stock market price [28]. In chemical industry, neural network was used to predict the performance of the fuel cell by comparative study [29]. And related work [30] used RBF neural network in engineering. Neural network were also frequently used in disease diagnosis. In [31], Aoe et al. applied neural network to deal with medical big data. For better diagnosis, they used deep learning to extract features of neuroimaging signals unique to various neurological diseases. They also developed a novel deep neural network to classify multiple neurological diseases using resting-state MEG signals. This algorithm would be useful for developing a classifier that wound improve neurological diagnosis and allowed high specificity in identifying diseases. Shi et al. [32] used high-dimensional characteristic vectors and low-dimensional vectors as input and lung sounds categories as output, and applied BP neural network to carry out lung sounds recognition. They found the performance was well and got recognition accuracies of 82.5% and 92.5%.

III. Methodology

We organize this section into four main subsections. The first subsection illustrates the framework AR-ANN. The following subsections introduce about thyroid disease, association rule mining algorithm and BP neural network respectively.

A. *AR-ANN overview*

Knowledge discovery and diagnosis framework AR-ANN integrated association rule mining algorithm and artificial neural network is shown in Fig.1. In AR-ANN, association rule mining algorithms are used to mine disease knowledge. We summarize this knowledge and select most frequent attribute as AR-ANN attribute. Then BP neural network is used to diagnose thyroid disease. The framework is shown in Fig. 1.

Most feature selection methods, including chi-square test, relief algorithm, logistic regression, and so on, which select features by setting thresholds manually. However, we use thyroid disease knowledge mined by association rule mining algorithms as AR-ANN attribute. AR-ANN model compares with traditional doctors' summary of disease factors and it increases the accuracy of diagnosis actually.

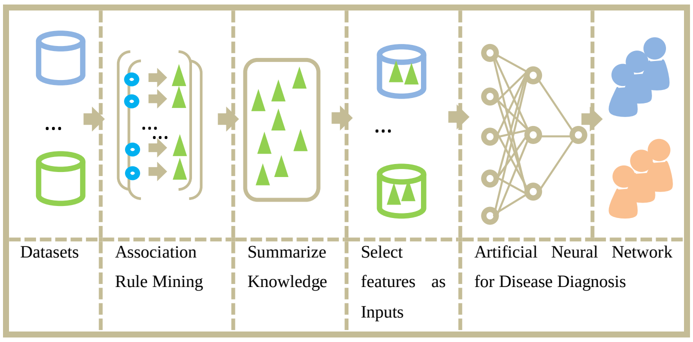


Fig.1. Framework of AR-ANN

B. *Classification of thyroid disease*

On November 30, 1984, the Thyroid Branch of the German Endocrine Society adopted a new classification standard for thyroid disease, which was divided into 1) hyperthyroidism 2) hypothyroidism 3) thyroiditis [33]. Another classification can be divided mainly into thyroid cyst and thyroid tumor, which seriously threaten health. This paper aims at mining association rule for thyroid disease data treated by medical treatment, and we use a uniform name below as thyroid disease.

C. *Association rule*

Association rule mining is a recognized data mining technology [34]. The form of the rule generated by the association learning is "LHS (left-hand-side) ⇒ RHS (right-hand-side)", where LHS and RHS are disjoint itemsets. This rule indicates that the RHS itemset is likely to occur whenever the LHS item set occurs. Support and Confidence are two indicators that measure the rules, which reflect the validity and certainty of the rules [35].

For the database transactions $D=\{I_1, I_2, I_3, \cdots, I_m\}$, let X, Y be an item, respectively, and $A \subset D$, $B \subset D$, $A \neq \emptyset$, $B \neq \emptyset, A \geq B$, then Rule $A \Rightarrow B$ is established in D, with Support and Confidence as follows(formula 1 and formula 2):

$$Support(X \leq Y) = P(X \cap Y) \tag{1}$$

$$Confidence(X \leq Y) = P(Y|X) = P(X \cap Y)/P(X) \tag{2}$$

Many association rule mining algorithms have been proposed, and the generated rules are different by different algorithms [36]. In this study, we focus on two popular algorithms, Apriori algorithm and Predictive Apriori algorithm.

i. *Apriori algorithm*

Apriori algorithm is one of the most influential mining algorithms for frequent itemsets [37]. In Apriori algorithm, the validity and authenticity of mining results largely depend on the choice of minimum support. Setting the minimum support too high or too low will affect the generated rules, and it is difficult to obtain satisfactory results without sufficient application experience. According to literature [38], we set the upper limit of minimum support to 0.2 in this paper, the lower limit of minimum support is set to 0.1, and the minimum confidence is set to 0.95.

ii. *Predictive Apriori algorithm*

The Predictive Apriori algorithm not only can extract the rules that a user are interested in, but also does not need to configure parameters such as minimum support and minimum confidence. Users only need to determine the number of interesting rules to be obtained [39]. The disadvantage of this algorithm is that it needs to scan the database continuously to calculate the support of itemsets with different lengths, and it is very time-consuming. In this algorithm experiment, the minimum accuracy is set to 0.99.

D. *Artificial Neural Network*

Artificial neural networks are common pattern recognition classifiers, and researchers have applied them to the research of medical big data [40]. In this paper, we use classical BP neural network to diagnose thyroid disease.

i. *BP neural network*

The BP neural network is a multi-layer feedforward neural network, which uses a gradient descent algorithm to achieve convergence. After the reverse weight correction, the final expectation is achieved. In this paper, we used the classical three-layer BP neural network including input layer, hidden layer and output layer. The structure is shown in Fig.2. In Fig.2, X_i and Y_i are the input and output values of the BP neural network respectively, and w_{ij} is the weight of the BP neural network. The hidden layer nodes are trained by the activation function.

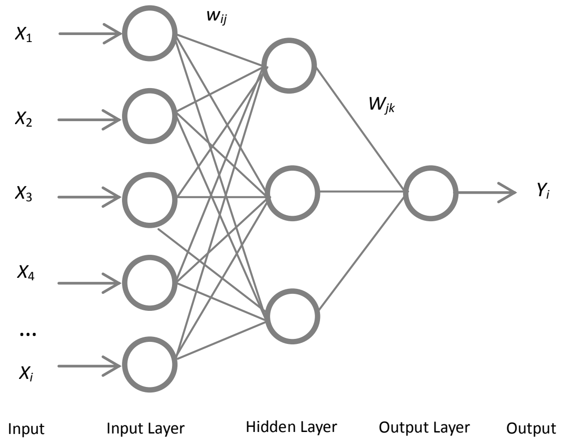


Fig.2. Structure of BP neural network

The disease diagnosis process by BP neural network is as follows. Dataset is divided into training set and test set. In the training phase, firstly BP neural network model is established. Secondly, input training set into the network. Then we train BP neural network until the number of iterations reaches the setting number or the training error reaches the minimum error. In the testing phase, the test set is input into the network to verify the learning ability of the model.

ii. *Selection of Activation Function*

The Activation Function can also be called Transfer Function. The selection of the activation function is an important part of the process of constructing a neural network. Five commonly used activation functions are introduced below (formula 3-7):

Liner Function

$$f(x) = k * x + c \tag{3}$$

Ramp Function

$$f(x) = \begin{cases} T, & x > c \\ k * x, & |x| \leq c \\ -T, & x <- c \end{cases} \tag{4}$$

Threshold Function

$$f(x) = \begin{cases} 0, & x < c \\ 1, & x \geq c \end{cases} \tag{5}$$

Sigmoid Function

$$f(x) = \frac{1}{1 + e^{-ax}} (0 < f(x) < 1) \tag{6}$$

Hyperbolic tangent sigmoid function

$$f(x) = \frac{2}{1 + e^{-2n}} - 1 \ (-1 < f(x) < 1) \tag{7}$$

IV. EXPERIMENTS

A. *Dataset overview*

Thyroid dataset involves sensitive personal information, and the most important thing in research is data-related privacy issue, which is also the core issue of data sharing in the era of healthcare and big data [41]. Therefore, this study uses two public thyroid datasets in the UCI machine learning repository, which are widely used by data mining researchers.

i. *Dataset preprocessing and feature selection*

As mentioned earlier, we use two public UCI thyroid datasets: sick dataset and sick-euthyroid dataset. And we delete the default value column. The sick dataset consists of a total of 29 attributes, and the sick-euthyroid dataset has 25 attributes. We choose 25 same attributes in both datasets. Then SPSS Statistics is used to preprocess the data, and the numerical data of age characteristics are transformed into nominal data. The numeric attribute is converted to a nominal attribute with an age range of 10. The details of 13 original attributes are shown in Table I. Parts of the experimental data which converted by SPSS Statistics is shown in Fig. 3.

TABLE I
ORIGINAL ATTRIBUTES

Attribute ID	Attribute Name	Attribute Explanation
1	*age_group*	Age interval
2	*sex*	M=Male or F=female
3	*on_thyroxine*	Whether taking thyroxine drugs, T=true or F=False
4	*query_on_thyroxine*	Whether taken thyroxine drugs T=true or F=False
5	*on_antithyroid_medication*	Whether taking anti-thyroid drugs T=true or F=False
6	*sick*	Whether sick T=true or F=False
7	*pregnant*	Whether pregnant T=true or F=False
8	*thyroid_surgery*	Whether in thyroid surgery T=true or F=False
9	*query_hypothyroid*	Whether had hypothyroidism T=true or F=False
10	*query_hyperthyroid*	Whether had hyperthyroidism T=true or F=False
11	*lithium*	Whether taking drugs containing lithium T=true or F=False
12	*goitre*	Whether have thyroid goitre T=true or F=False
13	*tumor*	Whether have thyroid tumor T=true or F=False
14	*class*	Health or sick

	age_group	sex	on_thyroxine	query_on_thyroxine	on_antithyroid_medicati...	sick	pregnant	thyroid_surgery	query_hypothyroid	query_hyperthyroid	lithium	goitre	tumor	class
1979	[60,70)	F	f	f	f	f	f	f	f	f	f	f	f	negative
1980	[60,70)	F	t	f	f	f	f	f	f	f	f	f	f	negative
1981	[60,70)	F	t	f	f	f	f	f	f	f	f	f	f	negative
1982	[60,70)	F	f	f	f	f	f	f	f	f	f	f	f	negative
1983	[60,70)	M	f	f	f	f	f	f	f	f	f	f	f	negative
1984	[60,70)	F	f	f	f	f	f	f	f	f	f	f	f	negative
1985	[60,70)	F	f	f	f	f	f	f	t	f	f	f	f	sick
1986	[60,70)	F	f	f	f	f	f	f	f	f	f	f	f	negative
1987	[60,70)	M	f	f	f	f	f	f	f	f	f	f	f	negative
1988	[60,70)	F	f	f	f	f	f	f	f	f	f	f	f	negative
1989	[60,70)	M	f	f	f	f	f	f	f	f	f	f	f	negative
1990	[60,70)	M	f	f	f	f	f	f	f	f	f	f	f	negative
1991	[60,70)	M	t	f	f	f	f	f	f	f	f	f	f	negative
1992	[60,70)	F	f	f	f	f	f	f	f	f	f	f	f	negative
1993	[60,70)	F	f	f	f	f	f	f	f	f	f	f	f	sick
1994	[60,70)	M	f	f	f	f	f	f	f	f	f	f	f	negative
1995	[60,70)	F	t	f	f	f	f	f	f	f	f	f	f	negative
1996	[60,70)	F	f	f	f	f	f	f	f	f	f	f	f	sick
1997	[60,70)	F	f	f	f	f	f	f	f	f	f	f	f	negative
1998	[60,70)	F	f	f	f	f	f	f	f	f	f	f	f	negative
1999	[60,70)	M	f	f	f	f	f	f	f	f	f	f	f	negative
2000	[60,70)	M	t	f	f	f	f	f	f	t	f	f	f	negative
2001	[60,70)	F	f	f	f	f	f	f	f	f	f	f	f	negative

Fig.3. Data preprocessing by SPSS Statistics

ii. *Application of Association rule mining algorithms in Thyroid Disease Data*

In this study, two datasets are analyzed by association rule mining algorithms, and all patients are divided into two categories, one belongs to the health, the other belongs to the sick. This study selects the Top-7 optimal rules for the Apriori algorithm with a confidence higher than 95% and an accuracy of higher than 99% in the Predictive Apriori algorithm. The first experiment sets the RHS to health and sick classification. The second experiment is to mine the association rules based on gender. The following subsections provide details of these experiments.

B. *Association rule mining to detect sick and healthy conditions*

i. *Rules extraction through Apriori algorithm mining*

In the first experiment, the generated rules by Apriori algorithm are shown in Table II. As the amount of healthy individuals is far more than sick individuals, we extract rules from sick classification independently. In sick dataset, the Top-7 association rules mined for healthy classification are all related to the age interval [50, 60), which indicates that people of 50 to 60 have more chance of being free from thyroid disease. And it is also an important indicator for healthy people that people have no history of hypothyroidism. The results indicate that when sick and pregnant are false, they are good indicators of a person being healthy. Rule 5 and Rule 6 describe that people from 50 to 60 are taking anti-thyroid drugs to keep healthy. This means these people have more chance of hyperthyroidism. Lithium is mentioned in rule 7, so the middle-aged people from 50 to 60 needs to pay attention to lithium intake. Rules mined for sick class indicated that the elderly from 60 to 70 are at lower risk of developing thyroid disease.

In sick-euthyroid dataset, all the rules for healthy classification describe that people are taking medications containing thyroxine to decrease the risk of thyroid disease, and the main role of thyroxine-containing drugs is to promote thyroxine, at the same time, people taking this kind of drugs may be treated with surgical thyroid disease (normal thyroid function). Therefore, we can't mine interesting knowledge for healthy classification. Considering the sick classification, the two factors, i.e. age interval [70, 80) and females, are found to be the most significant risk factors contribute to thyroid disease.

ii. *Rules extraction through Predictive Apriori algorithm mining*

As mentioned earlier, unlike Apriori based on the confidence, Predictive Apriori algorithm is based on accuracy and gives different results. The rules are shown in Table III.

In healthy classification, five of the seven rules generated by sick dataset indicate that young people are at less risk of developing thyroid disease, especially for women. Rule 7 describes all 13 factors indicate healthy classification. This means men from 50 to 60 have more factors contribute to thyroid disease than women. The rules generated by sick-euthyroid dataset for healthy classification are as follows. As described, many young women are at lower risk of thyroid disease. In rule 3, the rule mined for healthy classification of pregnant women does not match the clinical phenomenon. According to the literature [42], if non-pregnant women are used as diagnostic indicator, pregnant women are often missed due to loopholes in the thyroxine reference interval.

In general, the two algorithms generate different rules. However, the above results show that [60, 80) is high-incidence age interval for thyroid disease, and next is for middle-aged people. The factor of 'query_hypothyroid is false' is possible good factor for middle-aged people of [50, 60). In addition, young women have more chance of being free from thyroid disease, and elderly women [70, 80) have great risk of thyroid disease. Since the effects of gender on thyroid disease in these two subsections are not very specific, the next subsection will further investigate how gender impact thyroid disease as a contributing factor. Between two algorithms, the Apriori algorithm is more efficient and runs much faster than the Predictive Apriori algorithm. And the generated rule also shows a significant association. Therefore, Apriori algorithm is selected as the rule mining algorithm in the next subsection.

TABLE II
TOP-7 RULES GENERATED BY APRIORI ALGORITHM

Dataset		Rules	Confidence
sick		Healthy rules:	
	1.	age_group=[50,60) ∩ sick=f ∩ query_hypothyroid=f ==> class= health	0.97
	2.	age_group=[50,60) ∩ sick=f ∩ pregnant=f ∩ query_hypothyroid=f ==> class= health	0.97
	3.	age_group=[50,60) ∩ query_hypothyroid=f ==> class= health	0.97
	4.	age_group=[50,60) ∩ pregnant=f ∩ query_hypothyroid=f ==> class= health	0.97
	5.	age_group=[50,60) ∩ on_antithyroid_medication=f ∩ query_hypothyroid=f ==> class= health	0.97
	6.	age_group=[50,60) ∩ on_antithyroid_medication=f ∩ pregnant=f ∩ query_hypothyroid=f==> class= health	0.97
	7.	age_group=[50,60) ∩ query_hypothyroid=f ∩ lithium=f ==> class= health	0.97
		Sick rules:	
	1.	age_group=[60,70) ∩ query_ hyperthyroid=f ==> class=sick	1
	2.	age_group=[60,70) ∩ on_thyroxine=f ∩ query_on_thyroxine=f ==> class=sick	1
	3.	age_group=[60,70) ∩ on_thyroxine=f ∩ query_hyperthyroid=f ==> class=sick	1
	4.	age_group=[60,70) ∩ on_antithyroid_medication=f ∩ query_hyperthyroid=f==>class=sick	1
	5.	age_group=[60,70) ∩ pregnant=f ∩ query_hyperthyroid=f ==> class=sick	1
	6.	age_group=[60,70) ∩ thyroid_surgery=f ∩ query_hyperthyroid=f ==> class=sick	1
	7.	age_group=[60,70) ∩ query_hyperthyroid=f ∩ lithium=f ==> class=sick	1
sick-euthyroid		Healthy rules:	
	1.	on_thyroxine=t ∩ query_hyperthyroid=f ==> class= health	0.97
	2.	on_thyroxine=t ∩ query_hyperthyroid=f ∩ lithium=f ==> class= health	0.97
	3.	on_thyroxine=t ∩ query_hyperthyroid=f ∩ sick=f ==> class= health	0.97
	4.	on_thyroxine=t ∩ query_hyperthyroid=f ∩ sick=f ∩ lithium=f ==> class= health	0.97
	5.	on_thyroxine=t ==> class= health	0.97
	6.	on_thyroxine=t ∩ lithium=f ==> class= health	0.97
	7.	on_thyroxine=t ∩ sick=f ==> class= health	0.97
		Sick rules:	
	1.	age_group=[70,80) ∩ sex=F ∩ on_thyroxine=f ∩ query_on_thyroxine=f ∩ tumor=f==> class=sick	1
	2.	age_group=[70,80) ∩ sex=F ∩ on_thyroxine=f ∩ thyroid_surgery=f ∩ query_hypothyroid=f==> class=sick	1
	3.	age_group=[70,80) ∩ sex=F ∩ on_thyroxine=f ∩ thyroid_surgery=f ∩ query_hyperthyroid=f==> class=sick	1
	4.	age_group=[70,80) ∩ sex=F ∩ on_thyroxine=f ∩ query_hypothyroid=f ∩ tumor=f==> class=sick	1
	5.	age_group=[70,80) ∩ sex=F ∩ on_thyroxine=f ∩ query_hyperthyroid=f ∩ tumor=f ==> class=sick	1
	6.	age_group=[70,80) ∩ sex=F ∩ thyroid_surgery=f ∩ query_hypothyroid=f ∩ query_hyperthyroid=f==> class=sick	1
	7.	age_group=[70,80) ∩ sex=F ∩ thyroid_surgery=f ∩ query_hypothyroid=f ∩ tumor=f==> class=sick	1

TABLE III
TOP-7 RULES GENERATED BY PREDICTIVE APRIORI ALGORITHM

Dataset		Rules	Accuracy
sick		Healthy rules:	
	1.	age_group=[30,40) ∩ sex=F ∩ query_hypothyroid=f ==> class= health	0.99497
	2.	age_group=[30,40) ∩ sex=F ==> class= health	0.99489
	3.	age_group=[20,30) ∩ sex=F ==> class= health	0.99474
	4.	sex=F ∩ on_thyroxine=t ∩ query_on_thyroxine=f ∩ query_hypothyroid=f ==> class= health	0.9947
	5.	age_group=[30,40) ∩ on_thyroxine=f ∩ query_on_thyroxine=f ∩ on_antithyroid_medication=f ∩ sick=f ∩ query_hypothyroid=f ∩ goitre=f ==> class= health	0.99467
	6.	age_group=[30,40) ∩ on_thyroxine=f ∩ query_on_thyroxine=f ∩ query_hypothyroid=f ∩ goitre=f ∩ tumor=f ==> class= health	0.99467
	7.	age_group=[50,60) ∩ sex=M ∩ on_thyroxine=f ∩ query_on_thyroxine=f ∩ on_antithyroid_medication=f ∩ sick=f ∩pregnant=f ∩ thyroid_surgery=f ∩ query_hypothyroid=f ∩ query_hyperthyroid=f ∩ lithium=f ∩ goitre=f ∩ tumor=f ==> class= health	0.99248
sick-euthyroid		Healthy rules:	
	1.	age_group=[10,20) ∩ sex=F ==> class= health	0.99447
	2.	age_group=[20,30) ∩ sex=F ∩ on_thyroxine=f ==> class= health	0.99434
	3.	pregnant=t ==> class= health	0.99397
	4.	age_group=[30,40) ∩ on_thyroxine=t ==> class= health	0.99397
	5.	age_group=[20,30) ∩ sex=F ∩ query_on_thyroxine=f ∩ thyroid_surgery=f ==> class= health	0.99317
	6.	age_group=[40,50) ∩ query_hyperthyroid=t ==> class= health	0.99266
	7.	sex=F ∩ goitre=t ==> class= health	0.99228

C. *Apriori algorithm mining to detect gender conditions*

In the previous subsection, rules attributed to both genders are not very specific. In this subsection, the dataset will be split according to the factors of males and females, and the rules for sick classification and healthy classification will be extracted again. The effect of gender on thyroid disease will be studied in more details. In this experiment, the factors of gender and pregnant are removed in male group and the factor of gender is removed in female group. Based on the conclusions above, this subsection uses only the Apriori algorithm to extract the rules for males and females. The aim is to separately observe which factors are significantly related to thyroid disease in men and women. The rule extractions are shown in Table IV and Table V.

From Table IV and Table V, it is confirmed again that the elderly are most likely to suffer from thyroid disease, and next is middle-aged people. In addition, the middle-aged man [50, 60) who has history of thyroid disease needs to pay attention to the recurrence of thyroid disease. For women, half rules are attributed to take thyroxine drugs to maintain their health. This also shows that women are more likely to have hypothyroidism than men. In addition to age, 'sick is false', 'on antithyroid medication is false', 'on thyroxine is false', and 'pregnant is false' are good indicators.

TABLE IV
TOP-7 RULES GENERATED BY APRIORI ALGORITHM IN SICK DATASET

Gender	Rules		Confidence
Male	Healthy rules:		
	1.	age_group=[50,60) ∩ query_hypothyroid=f ==> class= health	0.99
	2.	age_group=[50,60) ∩ query_hypothyroid=f ∩ lithium=f ==> class= health	0.99
	3.	age_group=[50,60) ∩ on_antithyroid_medication=f ∩ query_hypothyroid =f ==>class= health	0.99
	4.	age_group=[50,60) ∩ query_hypothyroid=f ∩ tumor=f ==> class= health	0.99
	5.	age_group=[50,60) ∩ on_antithyroid_medication=f ∩ query_hypothyroid=f ∩ lithium=f ==> class=negative	0.99
	6.	age_group=[50,60) ∩ query_hypothyroid=f ∩ lithium=f ∩ tumor=f ==> class=negative	0.99
	7.	age_group=[50,60) ∩ thyroid_surgery=f ∩ query_hypothyroid=f ==> class=negative	0.99
	Sick rules:		
	1.	age_group=[80,90) ==> class=sick	1
	2.	age_group=[60,70) ∩ sick=f ==> class=sick	1
	3.	age_group=[80,90)∩ on_thyroxine=f ==> class=sick	1
	4.	age_group=[80,90) ∩ query_on_thyroxine=f ==> class=sick	1
	5.	age_group=[80,90) ∩ on_antithyroid_medication=f ==> class=sick	1
	6.	age_group=[80,90) ∩ thyroid_surgery=f ==> class=sick	1
	7.	age_group=[80,90) ∩ query_hypothyroid=f ==> class=sick	1
Female	Healthy rules:		
	1.	age_group=[50,60) ==> class= health	0.95
	2.	age_group=[50,60) ∩ pregnant=f ==> class= health	0.95
	3.	age_group=[50,60) ∩ on_antithyroid_medication=f ==> class= health	0.95
	4.	age_group=[50,60) ∩ on_antithyroid_medication=f ∩ pregnant=f ==> class= health	0.95
	5.	age_group=[60,70) ∩ sick=f ==> class= health	0.95
	6.	age_group=[60,70) ∩ on_antithyroid_medication=f ∩ sick=f ==> class= health	0.95
	7.	age_group=[60,70) ∩ sick=f ∩ pregnant=f ==> class= health	0.95
	Sick rules:		
	1.	age_group=[60,70) ==> class=sick	1
	2.	age_group=[60,70)∩ on_thyroxine=f ==> class=sick	1
	3.	age_group=[60,70) ∩ on_antithyroid_medication=f ==> class=sick	1
	4.	age_group=[60,70) ∩ pregnant=f ==> class=sick	1
	5.	age_group=[60,70)∩ thyroid_surgery=f ==> class=sick	1
	6.	age_group=[60,70) ∩ lithium=f ==> class=sick	1
	7.	age_group=[60,70) ∩ goitre=f ==> class=sick	1

TABLE V
TOP-7 RULES GENERATED BY APRIORI ALGORITHM IN SICK-EUTHYROID DATASET

Gender	Rules		Confidence
Male	Healthy rules:		
	1.	age_group=[50,60) ∩ query_hyperthyroid=f ==> class= health	0.94
	2.	age_group=[50,60) ∩ query_hyperthyroid=f ∩ lithium =f ==> class= health	0.94
	3.	age_group=[50,60) ∩ query_hyperthyroid=f ∩ goitre=f ==> class= health	0.94
	4.	age_group=[50,60) ∩ query_hyperthyroid=f ∩ lithium=f ∩ goitre=f ==> class= health	0.94
	5.	age_group=[50,60) ∩ on_antithyroid_medication=f ∩ query_hyperthyroid=f ==> class= health	0.94
	6.	age_group=[50,60) ∩ on_antithyroid_medication=f ∩ query_hyperthyroid=f ∩ lithium=f ==> class= health	0.94
	7.	age_group=[50,60) ∩ on_antithyroid_medication=f ∩ query_hyperthyroid=f ∩ goitre=f ==> class= health	0.94
	Sick rules:		
	1.	age_group=[60,70) ==> class=sick	1
	2.	age_group=[60,70) ∩ on_antithyroid_medication=f ==> class=sick	1
	3.	age_group=[60,70) ∩ thyroid_surgery=f ==> class=sick	1
	4.	age_group=[60,70) ∩ query_hypothyroid=f ==> class=sick	1
	5.	age_group=[60,70) ∩ query_hyperthyroid=f ==> class=sick	1

	6.	age_group=[60,70) ∩ lithium=f ==> class=sick	1
	7.	age_group=[60,70) ∩ on_antithyroid_medication=f ∩ thyroid_surgery=f ==> class=sick	1
Female	Healthy rules:		
	1.	on_thyroxine=t ∩ thyroid_surgery=f ∩ query_hypothyroid=f ∩ query_hyperthyroid=f ==> class= health	0.98
	2.	on_thyroxine=t ∩ thyroid_surgery=f ∩ query_hypothyroid=f ∩ query_hyperthyroid=f ∩ tumor=f ==> class= health	0.98
	3.	on_thyroxine=t ∩ thyroid_surgery=f ∩ query_hypothyroid=f ∩ query_hyperthyroid =f ∩ lithium=f ==> class= health	0.98
	4.	on_thyroxine=t ∩ thyroid_surgery=f ∩ query_hypothyroid=f ∩ query_hyperthyroid=f ∩ tumor=f ∩ lithium=f ==> class= health	0.98
	5.	on_thyroxine=t ∩ thyroid_surgery=f ∩ query_hypothyroid=f ∩query_hyperthyroid=f ∩ sick=f ==> class= health	0.98
	6.	on_thyroxine=t ∩ thyroid_surgery=f ∩ query_hypothyroid=f ∩ query_hyperthyroid=f ∩ sick=f ∩ tumor=f ==> class= health	0.98
	7.	on_thyroxine=t ∩ thyroid_surgery=f ∩ query_hypothyroid=f ∩ query_hyperthyroid=f ∩ sick=f ∩ lithium=f ==> class=health	0.98
	Sick rules:		
	1.	age_group=[60,70)==> class=sick	1
	2.	age_group=[80,90)==> class=sick	1
	3.	sick=t ==> class=sick	1
	4.	age_group=[60,70) ∩ on_antithyroid_medication=f ==> class=sick	1
	5.	age_group=[60,70) ∩ thyroid_surgery=f ==> class=sick	1
	6.	age_group=[60,70) ∩ pregnant=f ==> class=sick	1
	7.	age_group=[60,70) ∩ tumor=f ==> class=sick	1

D. *AR-ANN for disease diagnosis*

i. *Experiment setups*

In this experiment, we use MATLAB 2016a to build the model. The maximum number of iteration, the expected error, and the learning rate are respectively set to 1000, 0.2 and 0.001. The performance evaluation indicator is mean square error (MSE).

ii. *Selection and expression of inputs and outputs*

Based on the above-mentioned association rules, this subsection will filter attributes of the original experiment. Eight most frequent factors with five clinical test indicators (*TSH*, *T3*, *TT4*, *T4U*, *FTI*) are as the attributes of AR-ANN, and the original attributes with five clinical test indicators (*TSH, T3, TT4, T4U, FTI*) are as the attributes of baseline in this subsection. Outputs are results of diagnosis. The AR-ANN attributes are shown in Table VI.

iii. *Division of datasets*

Considering that the healthy individuals are far more than the sick individuals, we split the dataset into two parts that make two individuals almost have the same amount in these two parts. For sick dataset, 973 patients' data are used as training neural network model, and 974 patients' data are used as testing model performance. For sick-euthyroid dataset, 1000 patients' data are used as training neural network model, and 1000 patients' data are used as testing model performance.

iv. *Structure design of BP neural network*

In our experiment, the basic three-layer BP neural network is used to diagnose thyroid disease. In sick dataset, the neural nodes of input layer, hidden layer and output layer are 18, 10 and 1 respectively. In sick-euthyroid dataset, the neural nodes of input layer, hidden layer and output layer are 13, 10 and 1 respectively.

TABLE VI
AR-ANN ATTRIBUTES

Attribute ID	Attribute Name	Attribute Explanation
1	*age*	Age interval
2	*sex*	M=Male or F=female
3	*on_thyroxine*	Whether taking thyroxine drugs T=true or F=False
4	*on_antithyroid_ medication*	Whether taking anti-thyroid drugs T=true or F=False
5	*sick*	Whether sick T=true or F=False
6	*pregnant*	Whether pregnant T=true or F=False
7	*query_hypothyroid*	Whether had hypothyroidism T=true or F=False
8	*query_hyperthyroid*	Whether had hyperthyroidism T=true or F=False
9	*TSH*	Diagnostic indicators of thyroid disease
10	*T3*	Diagnostic indicators of thyroid disease
11	*TT4*	Diagnostic indicators of thyroid disease
12	*T4U*	Diagnostic indicators of thyroid disease
13	*FTI*	Diagnostic indicators of thyroid disease
14	*class*	Health or sick

v. *Selection of network algorithm and Activation Function*

In this paper, we choose Levenberg-Marquardt training algorithm, which is the fastest training algorithm for medium-scale networks. The activation function selects hyperbolic tangent logic function.

vi. *Results and analysis*

In this subsection, we apply four performance metrics to evaluate the results. Comparing with AR-ANN, the baseline method is without the pre-process of attribute filtering. The performance metrics are as follows.

Accuracy

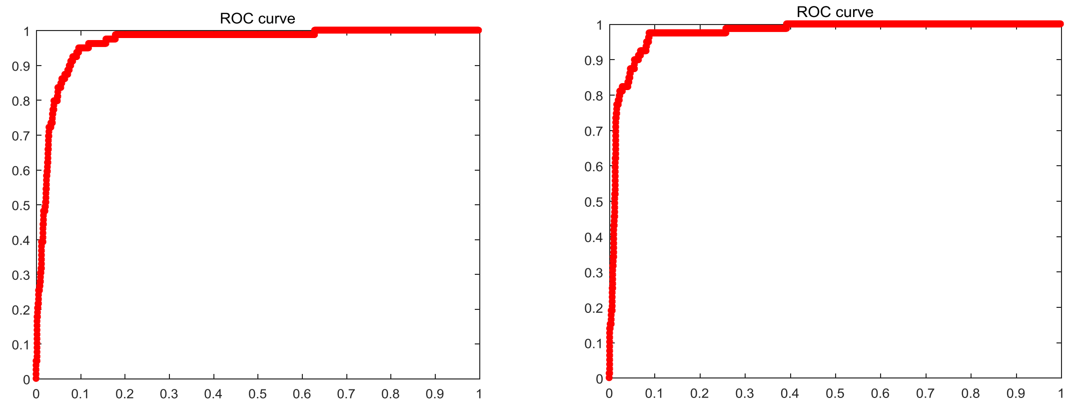
Accuracy is the proportion of true results among the total number of cases examined. The accuracies of BP neural network model which trained in two different datasets are in Table VII. In sick dataset, the accuracies are 0.9394 in baseline and 0.9558 in AR-ANN respectively, and the accuracies are 0.9330 and 0.9470 respectively in sick-euthyroid dataset. Based on these experimental results, it can be seen that the accuracy of AR-ANN is about one percent higher than baseline on average in both datasets. This means that the AR-ANN has always achieved a better performance in diagnosis prediction of thyroid disease.

ROC curve and AUC value

ROC (Receiver Operating Characteristic) curves of two datasets are shown in Fig.4 and Fig.5. The ROC curve is a plot over the set of predictions, which the abscissa is false positive rate (FPR), and the ordinate is true positive rate (TPR). Fig.4 (b) and Fig.5 (b), which are ROC curves from AR-ANN, have larger areas under the curve than Fig.4 (a) and Fig.5 (a) respectively. As the figures suggest, it can obtain better performance when attributes are filtered by association rule mining algorithm, i.e. Apriori. The corresponding AUC (Area under Curve) values are shown in Table VIII. Meanwhile, AUC value is defined as the area enclosed by the coordinate axis under the ROC curve. According to the corresponding AUC values of these figures, we can see that AUC values after filtering attributes are always at a higher level. A remarkably large improvement is obtained in sick-euthyroid dataset, and AUC value increases more obviously, which is increased by 0.0445. In sick dataset, it is only improved by one percentage point.

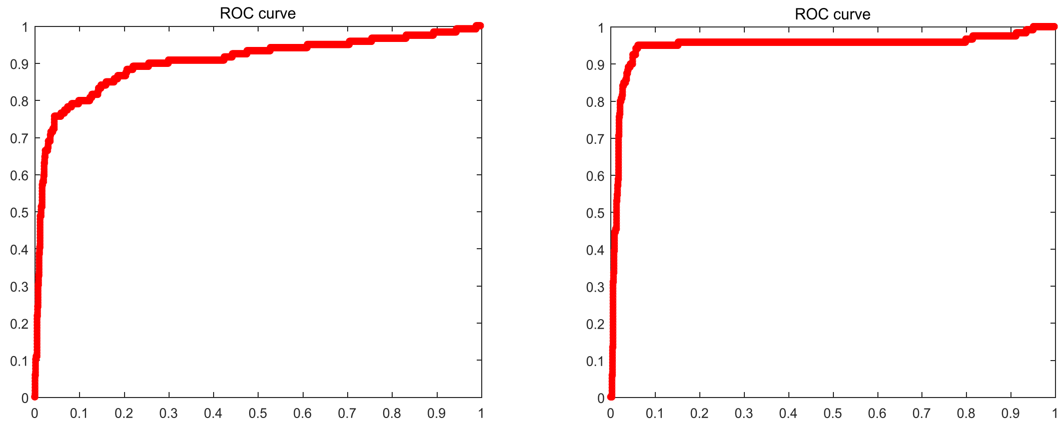
TABLE VII
DISEASE CLASSIFICATION IN TERMS OF ACCURACY

Datasets	Methods	Accuracy
sick	baseline	0.9394
	AR-ANN	0.9558
sick-euthyroid	baseline	0.9330
	AR-ANN	0.9470



(a) Baseline (b) AR-ANN

Fig.4. ROC curve obtained by using sick dataset



(a) Baseline (b) AR-ANN

Fig.5. ROC curve obtained by using sick-euthyroid dataset

TABLE VIII
AUC VALUE OF EXPERIMENTS

Datasets	Methods	AUC
sick	baseline	0.9623
	AR-ANN	0.9727
sick-euthyroid	baseline	0.9013
	AR-ANN	0.9458

Compare with other different methods

For accuracy comparisons among AR-ANN and other classification algorithms, we choose four other thyroid disease datasets in UCI machine learning repository (i.e. allhyper, allhypo, dis and hypothyroid). And the experimental results are reported in Table IX. As the table described, the performance of AR-ANN is superior to those obtained by other classifiers (i.e. Naive Bayes, KNN and SMO). In particular, AR-ANN achieves an average accuracy of 0.9631, while the classifiers of Naive Bayes, KNN and SMO just get 0.9404, 0.9432 and 0.9306 respectively. And AR-ANN achieves an accuracy of 0.9833 in dis dataset, which reports the highest accuracy among different datasets and classifiers. Overall, AR-ANN always has the highest accuracy in each dataset, but some results perform slightly better. The accuracies in allhyper dataset are almost the same among different methods, which are 0.97 on average. In hypothyroid dataset, the classification result of AR-ANN is very close to Naive Bayes classifier (accuracy of 0.9773 vs. 0.9720), and in dis dataset, the difference is only 0.02 with KNN classifier. While in sick, sick-euthyroid and allhypo datasets, we can see that AR-ANN significantly outperforms all the other three methods, and especially in sick-euthyroid dataset, the classification accuracy of AR-ANN is about six percent higher than SMO classifier.

TABLE IX
EXPERIMENTAL RESULTS OF EACH COMPARING METHODS

Datasets	Methods' Accuracy			
	AR-ANN	Naive Bayes	KNN	SMO
sick	0.9558	0.9305	0.9396	0.9169
sick-euthyroid	0.9330	0.8809	0.8853	0.8706
allhyper	0.9791	0.9731	0.9772	0.9731
allhypo	0.9502	0.9332	0.9147	0.9096
dis	0.9833	0.9516	0.9815	0.9784
hypothyroid	0.9773	0.9720	0.9610	0.9350

Friedman Test and Nemenyi Test

To evaluate the relative performance among the methods above, Friedman Test and Nemenyi Test are applied. For the two tests, we rank the performance of different methods in Table X. If different methods have the same performance, we assign the rank of values equally.

TABLE X
THE RANK OF COMPARING METHODS

Datasets	Ranks			
	AR-ANN	Naive Bayes	KNN	SMO
sick	1	3	2	4
sick-euthyroid	1	3	2	4
allhyper	1	3.5	2	3.5
allhypo	1	2	3	4
dis	1	4	2	3
hypothyroid	1	2	3	4
average ranks	1	2.9	2.3	3.8

Given k comparing methods and N data sets, let r_i be the average of the rank of the ith data set. Then the Friedman statistic τ_F can be calculated by formula (8) and (9). According to the F-distribution with (k-1) numerator degrees of freedom and (k-1)*(N-1) denominator degrees of freedom, the critical value is 3.287 at significance level α=0.05. In the comparison, the null hypothesis is clearly rejected. So we need proceed with a post-hoc test, which is Nemenyi Test, to analyze the relative performance by formula (10). For our test, q_α=2.569 at significance level α=0.05. Thus CD=1.9. The CD diagram on each evaluation criterion is shown in Fig.6, and we can see that AR-ANN is not connected with Naive Bayes and SMO except KNN, which means that AR-ANN is significantly superior to Naive Bayes and SMO, but in some datasets, AR-ANN has similar performance with KNN. And the experimental results also show that there is no significant difference among Naive Bayes, KNN and SMO.

$$\tau_{\chi^2} = \frac{12N}{k(k+1)}\left(\sum_{i=1}^{k} r_i^2 - \frac{k(k+1)^2}{4}\right) \tag{8}$$

$$\tau_F = \frac{(N-1)\tau_{\chi^2}}{N(k-1)-\tau_{\chi^2}} \tag{9}$$

$$CD = q_\alpha\sqrt{k(k+1)/6N} \tag{10}$$

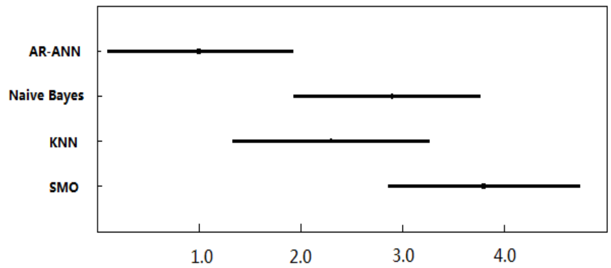


Fig.6 Friedman Test chart

V. CONCLUSIONS AND FUTURE WORK

In this paper, we firstly use the association rule mining algorithms to extract available rules in thyroid datasets for health and sick classification. Secondly, according to the factor of gender, the rules are further mined and studied in more details. Through extracted rules, it is found that the risk of thyroid disease increases with age, and the elderly (60-90) are most likely to suffer from thyroid disease. Then middle-aged men (50-60) who have no history of thyroid disease have more chance of being free from the recurrence of thyroid disease. If the elderly are sick, adequate prevention of thyroid disease should be done. In terms of gender, women are at higher risk of hypothyroidism than men. Among young people, women have less risk level than men. The aforementioned conclusions show that gender and age are two most important factors leading to thyroid disease. These are also supported by existing clinical medical research. In future experimental research, gender and age should be listed as important factors impacting thyroid disease.

Finally, the BP neural network model is established to diagnose the thyroid disease. The experimental results show that the model performance is very good, and it also preliminarily illustrates the feasibility and practical value of association rule mining algorithm and BP neural network in medical aided diagnosis.

In general, different patients have different factors contributed to thyroid disease. Datasets used in this paper still have some limitations on this research, including geography, climate, and so on. In addition, the small dataset is also a problem. Knowledge mined through thyroid disease datasets in our paper may be inconsistent with local thyroid disease factors, but also prove some clinical guesses.

Overall, the diagnosis framework AR-ANN of thyroid disease established in this paper has only done some qualitative basic work. Therefore, to develop more powerful model is our core task, and there are many factors, which are my future work: the choice of artificial neural network type, the number of hidden layers and hidden layers neural nodes, training functions, and so on.

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