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ORIGINAL ARTICLE

Confirmation of the abnormal lipid metabolism as a risk factor for the disease of leukoaraiosis

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Abstract Our purpose is to screen out medical history indicators and test indicators linked to lipid metabolism which is closely correlated to leukoaraiosis (LA), and to build assistant diagnosis model based on support vector machine (SVM), which provided theoretical evidence for genesis and development of LA. One thousand LA patients who underwent magnetic resonance imaging (MRI) examination in Imaging Department was retrospectively analyzed and divided into LA group and non-LA group in accordance with examination results. Detailed clinical statistics of the two groups were collected, including test indicators related to lipid metabolism, such as total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), medical history indicators, age, sex, diabetes, hypertension, hyperlipidemia, history of intracranial infection, history of cerebral hemorrhage, cerebral infarction, lacunar infarction and relevant biochemical indexes. The study shows that patients' incidence of LA was 31.10%; in accordance with Logistic analysis, the incidence of LA is significantly correlated to factors like age, hypertension, history of cerebral hemorrhage, cerebral infarction, lacunar infarction and triglyceride elevation; two SVMs, one including all variables and the other containing all screened variables were successfully established, and the former's accuracy, specificity and sensitivity respectively were 85.0%, 85.0% and 85.0% while the latter's 90.0%, 100.0% and 80.0%. Test indicators and medical history indicators of lipid metabolism correlated to LA were screened out successfully. Meanwhile, an effective SVM model also was built successfully, which is able to predict LA relatively accurately and can be used as assistant diagnostic tool for clinicians.

1. Introduction

Hyperlipemia, known as dyslipidemia in modern medicine, is characterized by excessive total serum cholesterol and triglyceride (Kagoya et al., 2012). Due to no obvious symptoms and latent onset, hyperlipemia is called "the Silent Killer" in the field of medicine (Zhang, 2016) and it is generally found

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in physical examination. At present, serum total cholesterol (TC), triglyceride (TG), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C) are often used as test indicators of hyperlipidemia, any of which exceeding normal criteria is recorded as hyperlipidemia. Leukoaraiosis (LA), described in iconography, is a disease of abnormal changes in cerebral white matter. It is proposed in 1986 by the Canadian neurologist Hachinski et al. (1986). LA is often found in the medical examination of the elderly so it was believed that the disease was only related to age and drew little attention from people. But in fact, it is a clinical syndrome caused by a variety of pathogenesis (Huo and Feng, 2015). Pathological studies have shown that LA lesions are mainly caused by the changes of demyelination in white matter, which is expressed in CT as white matter mottling or diffuse low density image in periventricular and semi-oval central area (Huo and Feng, 2015), and in magnetic resonance imaging (MRI) showed isointense or hypointense on T1-weighted image and hyperintense on T2-weighted image. Studies have shown that LA is a biomedical marker for brain aging (Ross et al., 2005) and is closely correlated to Alzheimer (Guo et al., 2004; Pantoni et al., 2007). LA may be a different manifestation pattern of stroke in addition to causing slowed thinking, declined cognitive function and mental status changes (Hassan et al., 2004).

At present, there is no effective therapy for LA, thus how to prevent LA has been a hot research issue (Hassan et al., 2004; Culebras, 2004; Fujita et al., 2005; Altaf et al., 2006; Chen et al., 2004). Through looking for risk factors inducing LA and treating them targetedly can effectively prevent occurrence of dementia, stroke and death. This study established support vector machine (SVM) based on the risk factors inducing LA and provided certain theoretical basis for prevention of LA's genesis and development.

2. Materials and methods

2.1. Subjects

One thousand patients who received enhanced cranial plain scan MRI examination in Imaging Department from September 2010 to September 2015 were enrolled. According to the MRI findings and LA diagnostic criteria, patients were divided into LA group and non-LA group. After reading documents (Culebras, 2004; Fujita et al., 2005), reported pathogenesis of LA was combined with clinical experience to collect the possible factors related to LA. Finally, risk factors included in the study were age, sex, diabetes, hypertension, history of intracranial infection, cerebral hemorrhage, cerebral infarction as well as lacunar infarction, and test indicators linked to lipid metabolism (TC, TG, LDL and HDL). In addition, detailed medical history of each patient was inquired by the same neurologist, and MRI images of cerebral infarction and lacunar infarction were combined to collect materials of patients.

2.2. Variable definitions

① LA: LA is shown as the punctuate, patchy or fusion flaky long T1 and long T2 signals on MRI around the ventricle.

② Infarction: Infarction is shown as long T1 and long T2 signals on MRI with a diameter >5 mm.

③ Lacunar infarction: Lacunar infarction was shown as long T1 and long T2 signals on MRI with a diameter <15 mm: level 0 = no; level 1 = 1 ~ 3; level 2 = 4 ~ 10; level 3 = more than 10.

④ History of hypertension: According to the WHO/ISH *Guidelines and Reports of Hypertension* in 2007, Systolic Blood Pressure (SBP) $\geqslant$ 140 mmHg and/or Diastolic Blood Pressure (DBP) $\geqslant$ 90 mmHg and/or who are taking antihypertensive drugs are recorded as hypertension history.

⑤ Diabetes: The diagnostic standards of World Health Organization (WHO) about diabetes in 2005 are: showing diabetes symptoms and fasting blood-glucose $\geqslant$ 7.0 mmol/L (126 mg/dl), or blood glucose $\geqslant$ 11.1 mmol/L (200 mg/dl) 2 h after meal.

⑥ Hyperlipidemia: According to *Guidelines for Prevention and Treatment of Chinese Adult Dyslipidemia* in 2007, any terms exceeds the four following criteria can be recorded as hyperlipemia: TC $\geqslant$ 5.80 mmol/L, TG $\geqslant$ 1.80 mmol/L, LDL $\geqslant$ 3.60 mmol/L, HDL $\leqslant$ 1.00 mmol/L, any index from the above four terms excesses the standard will be decided as hyperlipidemia.

⑦ Cerebral hemorrhage history: Since a variety of causes lead to cerebral hemorrhage, all patients ever had the disease are recorded as a history of cerebral hemorrhage.

2.3. Statistical analysis

SPSS21.0 software was utilized for statistical analysis, χ^2 test was used for comparison and $P < 0.05$ was considered statistically significant.

2.4. Logistic regression analysis

Several risk factors of LA have been screened out with forward stepwise Logistic regression analysis by SPSS 21.0 software in this study.

2.5. SVM

Two assistant diagnostic models of LA based on all variables and screened variables respectively were established with SVM algorithm. Then the results were divided into two categories and each of them was randomly divided into two groups, one as training set and the other as test set. The SVM models were constructed by MATLAB software and evaluated in terms of accuracy, sensitivity and specificity.

3. Results

3.1. The incidence of LA

According to the analysis of 1000 patients' clinical data, their incidence of LA was 30.10% (311/1000). The percentage of patients who had diabetes, hypertension, hyperlipidemia, history of cerebral hemorrhage, cerebral infarction, lacunar infarction, triglyceride elevation in LA group was greater than that in non-LA group.