Applying the Logistic Regression Model to Predict the Stenosis in Carotid Artery Using the Sequential Color Doppler Ultrasound Image Processing

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Abstract

Background- Early detection of stenosis in carotid artery is essential because it directly affects the patients' clinical management and is of prognostic value. Therefore, estimating mechanical properties of this artery in normal and atherosclerosis cases is important as far as medical treatment is concerned. We applied a logistic regression model to predict carotid artery stenosis in a group of patients based on the quantitative features extracted from the processing of the conventional color Doppler ultrasound images.

Methods- Our database includes 128 patient records consisting 10 quantitative features. The database is then randomly divided into the training and validation samples including 98 and 30 patient records respectively. The training and validation samples are used to construct the logistic regression model and to validate its performance. Finally, important criteria such as sensitivity, specificity, accuracy and receiver operating characteristic curve (ROC) analysis for this method are evaluated.

Results- Our results show that the logistic regression model is able to classify correctly 28 out of 30 cases presented in the validation sample. The output of this method showed a high positive predictive value of 94%.

Conclusion- We have established a logistic discriminator approach which is able to predict the probability of stenosis in the carotid artery using features extracted from ultrasonic measurements on ultrasound imaging ***(Iranian Heart Journal 2008; 9 (2):43-50).***

Key words: color Doppler ultrasound ■ carotid artery stenosis ■ mechanical properties ■ logistic regression analysis

Stroke is one of the most common causes of death and disability in industrialized nations. Approximately 80% of ischemic strokes are due to athero-thromboembolic infarction, which is caused by atherosclerotic lesions at the carotid bifurcation.[1, 2]

Currently, the Doppler ultrasound technique is widely recognized as the best non-invasive screening test for carotid artery stenosis. Ultrasound does not calculate the degree of arterial narrowing directly, but relies on extrapolating changes in flow parameters to an anatomical stenosis.

Despite the availability of several qualitative and quantitative methods for the assessment of carotid artery stenosis, accurate diagnosis of stenosis remains a clinically difficult task.

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Conventional catheter angiography is therefore often performed for clinical confirmation. Although specific, catheter angiography is an invasive, costly, and psychologically stressful procedure. Estimation of arterial diameter throughout the carotid cycle has been conducted increasingly to study the mechanical properties of the arterial wall and changes associated with disease.

Arterial diameter, wall thickness, cross section changes, and blood pressure measurements can be used to calculate the stiffness indices of the common carotid artery. Several indices are used to evaluate the elastic properties of the common carotid artery including: distensibility, compliance, Young's modulus, and pressure-strain elastic modulus and stiffness indices.[3-5] Recently, there has been much interest on the relationship between arterial stiffness and cardiovascular diseases.[3, 6-14]

Consequently a computerized second opinion in the form of a logistic regression model could be useful for the differentiation of atherosclerosis from normal.

In this study we intended to establish a logistic regression model to work as a tool for radiologist to predict atherosclerotic disease in carotid artery using physical and mechanical parameters extracted by processing the sequential color Doppler ultrasound images.

The performance of the established model was then evaluated using the common statistical index positive predictive value and ROC analysis.[16, 17]

Methods

Our goal was to apply the logistic discriminant analysis to the data collected in a study designed to predict the carotid artery stenosis on the basis of features that had been extracted from measuring the ultrasonic tissue characteristics consisted of diastolic diameter, systolic diameter, pulse pressure, arterial strain, static pressure change on wall, peak systolic velocity, end diastolic velocity, pressure-strain elastic modulus, static pressure-strain elastic modulus[17] and stiffness. Our study group consisted of 128 men with mean age 66±11 years. These patients were studied from Nov 2000 to April 2004. Patients were categorized into two groups based on the results of angiography as well as clinical diagnosis. These two groups were; normal subjects (n=55) with no history of cardiovascular disease, cerebrovascular disease, hypertension and diabetes, and the patients of mild (<40%) or severe stenosis (>40%) with angiographically documented (n=73). All subjects underwent B-mode and color Doppler ultrasonography.

For each patient in our database we performed a complete examination including common, external and internal carotids. The ultrasonic examination of right common carotid artery was performed after at least 15 minutes rest in the supine position when the heart rate and blood pressure had reached a steady state. High-resolution B-mode ultrasound and color Doppler images from right common carotid artery were obtained with a 7.5 MHz linear array transducer attached to ultrasound machine (GE-logic-500 MD version 4, USA). A data acquisition system consisting of personal computer and multimedia board (Video-blaster SE Creative Technology) were used for monitoring and grabbing the changes in cross sectional area. For each ultrasound examination, matching longitudinal views of the common carotid artery were located. The frames which represent a minimum of two cardiac cycles were then grabbed. The cross sectional area of right common carotid artery was measured by color Doppler imaging throughout cardiac cycle. The computerized multi-frame image processing method was then applied to all of the obtained frames. This generated a sequence of cross sectional area of carotid artery measurement over two cardiac cycles. The maximum and minimum cross sectional area and wall thickness at the point of minimum cross sectional area of right common carotid artery were determined over each cardiac cycle. The carotid diameter was defined as the mean value of the maximum systolic diameter (D_s) and the minimum diastolic diameter (D_d). The diameters were calculated at a point approximately 2 cm proximal to the bifurcation based on the cross-section images of the right common carotid artery (Fig. 1) with Image Tool software (UTHSCSA Image Tool for Windows, version 3, USA).

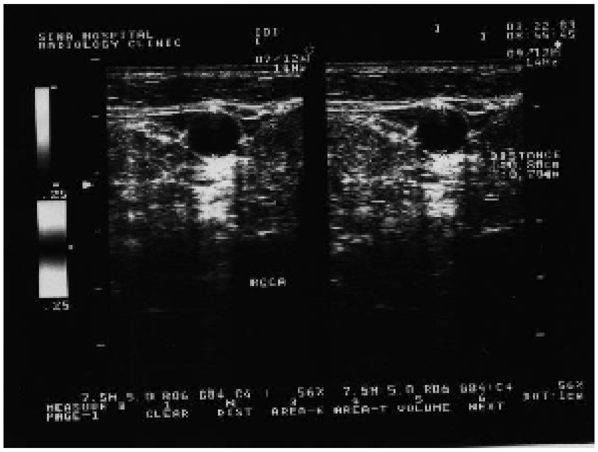

Fig. 1. B-mode image from cross section of common carotid artery throughout cardiac cycle.

These data was then used to calculate the arterial characteristics according to the papers.[5,18] Indeed, since the static pressure changes in arteries is associated with variation in blood flow velocities through cardiac cycle; we estimated the detailed static pressure changes (ΔP_s) by measuring the peak systolic velocity (PSV) (V_s) and end diastolic velocity (EDV) (V_d). From the strain and the pulse pressure measurements, pressure-strain elastic modulus (E_p) were defined as described by Peterson,[18] and from the strain and the static pressure changes, static pressure-strain elastic modulus (E_{ps}) were estimated.

The value of the stiffness (β) was therefore established as an estimate of vascular compliance,[19] using arterial relative diameter changes data. The details of measurement have been previously reported elsewhere.[17] Table I shows all the parameters in our database, which represented ultrasound measurements.

Table I. The extracted quantitative parameters the sequential color Doppler ultrasound image processing which used as input into the logistic regression model.

Indexes (unit)	**Mean ± S.D.**	**Range**
Minimum diastolic diameter (mm)	7.5± 0.9	6.0
Maximum systolic diameter (mm)	0.9±0.2	1.2
Pulse pressure (Pa)	6708.7±2122.2	13436.0
Arterial strain percent	7.9±3.5	16.9
Static pressure change (N/m^2)	244.0±121.1	671
Peak systolic velocity (cm/s)	70.3±19.3	103.7
End diastolic velocity (cm/s)	22.74±14.3	94.5
Pressure-strain elastic modulus (N/m^2)	117678.7±99635.4	735676.1
Static pressure-strain elastic modulus (N/m^2)	3668.1±2295.7	10473.1
Stiffness	6.8±3.6	21.8

We used logistic regression model as a classifier to predict the carotid artery stenosis. The training and validation samples were used to build and validate the logistic regression model, respectively. Briefly, the logistic regression analysis is a statistical technique through which one examines the relationship between a dependent variable (result of angiography represented by Y) and a set of independent variables (10 ultrasonic features represented by X1 to X10).

$$E\{Y\} = p = \frac{\exp(a + b_1 X1 + \ldots + b_{14} X10)}{1 + \exp(a + b_1 X1 + \ldots + b_{14} X10)}$$

Then the independent variables, which could provide the best prediction, will be selected.

This approach is commonly applied to predict membership in two groups using a set of predictors (n=10). Suppose we have two populations with different prior probabilities. Using the cases presented in the training samples (n=98) as well as the prior probability the posterior probabilities for each group was obtained. Then, the cases presented in the validation samples (n=30) are separated based on the obtained posterior probability associated with variables. The simplest optimizing method of discrimination is to maximize the posterior probability of correct allocation. To obtain the posterior probability the logit coefficients could be estimated using the Maximum Likelihood Estimation.[20] Allocation of new cases can be performed using logit function, which could be obtained using the natural logarithm of the ratio of the calculated posterior probabilities [21]:

$$\mathrm{Ln}\left({}^{P}\!/_{1-P}\right) = \mathrm{Logit}\ (p) = \alpha + \beta_1 X1 + \ldots + \beta_{14}\, X10$$

If the outcome of the logit function is positive (with the assumption of equal prior probabilities) the individual is allocated to class one (group which have the stenosis). On the other hand, if the outcome is negative, the case is allocated to class two (normal group). The features that entered into the allocation rule were selected by Wald statistics. It is the square of the ratio of the unstandardized logit coefficients to its standard error, which has a chi-square distribution.[21] We addressed a brief detail of logistic regression theory elsewhere.[22]

We initially used logistic regression analysis to predict the outcome of stenosis using a data base consisted of 128 patients' characteristics. We randomly selected 76% (n=98) of patient's records (including 56 from the initial stenosis group and 42 from normal group) to compose the estimation samples. To prepare the validation samples, the rest of data 24% (n=30) of patient's records (including 16 from the initial stenosis group and 14 from normal group) were selected. The dependent (criterion) variable was the dichotomized result of catheter angiography defined as normal (0) or stenosis.[1] The independent variables entered into the logistic regression equation were all evaluated parameters which represented in Table I. We computed a covariance matrix containing all continuous variables to fulfill the established guideline for feature selection. The analysis generated Wald statistics, regression coefficients, standard errors, confidence intervals, Nagelkerke R^2, Hosmer-Lemeshow goodness-of-fit chi square, and predicted group membership. The Nagelkerke R^2 attempts to quantify the proportion of explained variance in the logistic regression model, similar to the R^2 in linear regression, although the variation in a logistic regression model must be defined differently. Nagelkerke[23] proposed a modification to the Cox and Snell R^2 so that the value of 1 could be achieved. Ultimately, we built logistic regression models using forward stepwise procedure in SPSS statistical package (Version 10) based on MLE method.

Receiver Operating Characteristic (ROC) analysis is widely used to evaluate diagnostic performance of logistic discriminant. An ROC curve provides a concise description of trade-offs available between sensitivity and specificity. The area under an ROC curve, denoted A_z when the ROC curve is fitted with the conventional binomial model is often used to summarize the diagnostic performance described by entire ROC curve.[15,16,24]

After logistic discriminator approach had been established perfectly the validation samples was presented to the model giving two posterior probabilities. Taking into consideration the posterior probability of presence of stenosis, the diagnostic performance of the logistic discriminator approach was estimated. In this regard, the true positive and the false-positive fractions were determined. These data were then used to plot the ROC curves. Ultimately, the area under the ROC curve (A_z) was used to compare the performance of the logistic discriminator approach on validation samples (n=30) during the testing procedure. To evaluate the performance of the logistic discriminator approach, the obtained posterior probability of stenosis was classified into the five categories: output in the range of (0.0-0.2)=normal, (0.2-0.4)=slightly stenosis, (0.4-0.6)=mild stenosis, (0.6-0.8)=marked stenosis, (0.8-1) = severe stenosis.

Results

We ran a logistic regression model using a forward stepwise procedure. We used the likelihood-ratio (LR) test to enter variables into the model. Ten variables were entered into the training model before the forward stepwise procedure was terminated. Variables included in the logistic regression model were presented in Table I. The Nagelkerke R^2 for the logistic regression model was 0.909 at step 2 suggesting that 91% of the variance associated with result of angiography was accounted for in the model. The Hosmer-Lemeshow chi-square was 0.467 (*df*= 8, P=0.998). Table II shows the maximum likelihood estimates of the parameters, standard errors, Wald statistic and corresponding p-values of the logistic regression models fitted to the estimation samples (n=98) for the significant features at last step (step 2). The logistic regression equation for the statistically significant predictors was:

Logit(p) = -24.504+0.631×Strain percent + 0.007× the Static pressure-strain elastic modulus (N/m2)

Based on the established logit function an individual case presented in the validation samples is allocated to the stenosis group if the logit (p)>0; otherwise to normal group. The output of the logistic discriminant analysis on validation samples (Table II) showed a high positive predictive value (TP/TP+FP) of 94%.

Table II. Indicating the maximum likelihood estimates, standard errors, Wald statistic and corresponding p-values of the logistic regression model fitted to the estimation samples (n=98) for the significant parameters.

Variable	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square
Intercept	-24.504	8.196	8.939	.003
Strain percent	.631	.278	5.153	.023
Static pressure-strain elastic modulus	.007	.002	9.944	.002

A receiver operating characteristic (ROC) curve was computed using the predicted probabilities for group membership from the logistic regression model. Each point on the curve represents the true-positive rate (sensitivity) and the false-positive rate (1_specificity) for a single value. The area under the ROC curve (Fig. 2) based on the logistic regression model is 0.9471 (SE= 0.0276).

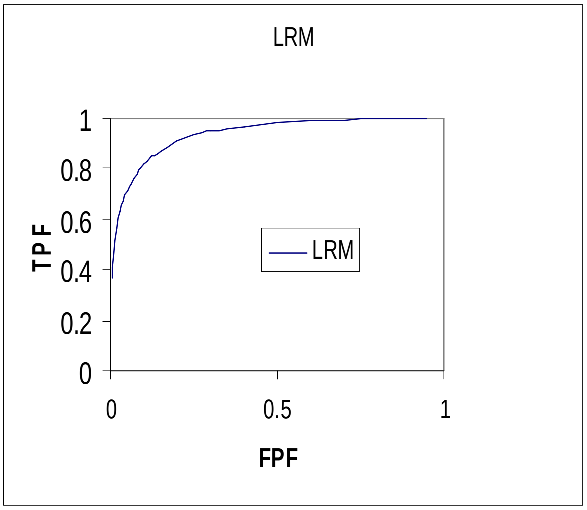

Fig. 2. Resulting ROC curve for the logistic regression discriminant model (LDM) on validation samples (n=30) demonstrating the diagnostic performance.

Discussion

There is an ongoing effort in field of radiology to establish non-invasive method for evaluation the risk of stenosis in order to avoid the disadvantages associated with the invasive methods such as the conventional catheter angiography. The emergence of new imaging techniques such as Doppler ultrasound technique that result in the production of large amounts of quantitative data justify more attention to be spent in this field. Currently, Doppler ultrasound technique is well-recognized as the best non-invasive screening test for carotid artery stenosis. Ultrasound calculates the degree of arterial narrowing indirectly by measuring the changes happened in flow parameters. It is currently the only modality to image arterial walls in real time with reasonable resolution. This will allow better observation of morphological, hemodynamic and elastic properties of tissue.[25] In addition, high-resolution B-mode imaging prepares better measure for the observation of carotid arterial structures including wall thickness, arterial diameter and stenosis. Numerous articles exist regarding the Doppler criteria for diagnosing stenosis/ occlusion. Furthermore, since the Doppler waveforms are affected by pathophysiological properties of the arterial system, they could therefore produce more useful information for cardiovascular assessment.[3, 26] Many reports support this hypothesis that many of these systematic risk factors predispose to atherosclerosis development and progression. This suggests that biomechanical factors, such as static pressure, wall shear stress, blood viscosity and flow velocity, may be responsible for the localization and progression of atherosclerosis. Arterial diameter changes and blood pressure measurements can be used to calculate elastic properties of common carotid artery. Several features mentioned in the literature which have some importance to evaluate elastic properties of the common carotid artery. These features were distensibility, compliance, Young's modulus, pressure-strain elastic modulus and stiffness indices.[25, 27, 28]

In the present study we assumed that applying the objective features extracted from ultrasonic measurement on ultrasound imaging and analyzed by a logistic discriminator approach can possibly help radiologist to predict the risk of stenosis. This assumption is justified because of the previous reports suggested the potential usefulness of the logistic discriminant analysis in making association between many independent continuous and qualitative features.[29] This happened by establishing similarities among evaluated features in the estimation samples during the estimation process by addressing them as proportional parameters. The estimated parameters were then used during the validation process to evaluate the probability of stenosis for the cases that have not been previously presented to the model. The best positive predictive value of the LRM on validation samples (n=30) was 94%.

In conclusion, we have established a logistic discriminantor approach which is able to predict the probability of stenosis in carotid artery using features extracted from ultrasonic measurement on ultrasound imaging. Four of the chief attractions of logistic discrimination are: (i) The model is simple and few distributional assumption are made. (ii) It is applicable with either continuous or discrete predictor variables, or both. (iii) It is very easy to use with fewer computation demands. (iv) Once the parameters have been estimated, the allocation of fresh individuals requires only the calculation of a linear function.

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