Classification Model for Cerebral Aneurysm Rupture Prediction using Medical and Blood-flow-simulation Data

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Abstract: Stroke is a serious cerebrovascular condition, in which brain cells die due to an abrupt blockage of arteries supplying blood and oxygen or due to bleeding in the brain tissue when a blood vessel bursts or ruptures. Because stroke occurs suddenly in most people, prevention is oftentimes difficult. In Japan, this condition is one of the major causes of death, which is associated with high medical cost, especially among the society's aging population. Therefore, stroke prediction and treatment is important. Stroke incidences can be avoided by a preventive treatment based on the risk of onset. However, since judgment of the onset risk largely depends on the individual experience and skill of the doctor, a highly accurate prediction method that is independent of the doctor's experience and skill is the focus of this study. The target of prediction for this research is subarachnoid hemorrhage that is part of stroke. Logistic regression and support vector machine that predict cerebral aneurysm rupture by machine learning using combined medical data and cerebral blood-flow-simulation data were employed to analyze 338 cerebral aneurysm samples (35 ruptured, 303 unruptured). SMOTE algorithm solved the imbalance of data, while the SelectKBest algorithm was used to extract important features from the total 70 features obtained from both data. Out of the 27 important features extracted, 40% belonged to the medical data and the remaining 60% were from the blood-flow-simulation data. Using logistic regression as a classification model, we found the sensitivity of 0.64 and the specificity of 0.85. The results validated the possibility of a highly accurate method of cerebral aneurysm rupture prediction by machine learning using engineering information obtained from mechanical simulation.

1 INTRODUCTION

Stroke—a generic term for cerebral infarction, cerebral hemorrhage, and subarachnoid hemorrhage—is a serious cerebrovascular condition, in which the brain cells die due to an abrupt blockage of arteries that supply blood and oxygen to the brain or due to bleeding in the brain tissue when a blood vessel bursts. For many people, stroke may occur suddenly and without warning; thus, it could be difficult to prevent. In Japan, stroke is one of the leading causes of death. In 2017, stroke became the country's third leading cause of death due to illness and the number one cause of being bedridden. Prediction and cure of the condition is an important issue. Reducing stroke incidence requires a preventive treatment that deals with the risk of onset; however, at present, risk judgment largely depends on the individual experience and skill of the doctor. Therefore, prediction of the onset of stroke that is highly accurate and independent of the doctor's experience and skill is required.

Existing stroke-prediction models (Manolio et al., 1996), (Lumley et al., 2002) adopted features that are clinically verified or manually selected by medical experts. (Wang et al., 2003), (Hitman et al., 2007), and (Letham et al., 2015) used medical history data as input features in their research, while (Amini et al., 2013) used K-nearest neighbor and C4.5 decision tree

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method on medical history data for stroke prediction. Moreover, some studies have started employing vascular imaging for disease prediction; for example, (Nogueira et al., 2016) employed vascular imaging to predict clinical outcomes and investigated the risk of symptomatic intracerebral hemorrhage in patients who underwent intravenous thrombolytic treatment. On the other hand, (Bentley et al., 2014) used computerized tomography brain-image inputs into a support vector machine (SVM) algorithm to predict stroke.

There are several other reports wherein the state of cerebral blood flow, in addition to medical information, was deeply involved with the stroke onset (Chung and Cebral, 2015). (Morino et al., 2010) used particle image velocimetry (PIV) and laser doppler velocimetry (LDV) to measure the velocity profiles of ruptured and unruptured intra-aneurysmal hemodynamics. (Xiang et al., 2014) examined how an inlet waveform affects the predicted hemodynamics in patient-specific aneurysm geometries. (Shojima et al., 2004), (Qian et al., 2011), and (Takao et al., 2012) acknowledged the importance of wall shear stress (WSS), energy loss (EL), and pressure loss coefficient (PLC), respectively, in predicting cerebral aneurysm rupture.

Among these studies, very few considered combining data from various technological sources to successfully predict a stroke onset. In this regard, this study combined medical data with blood-flow data obtained by computational fluid dynamics (CFD) simulations into a classification model for enhanced prediction. Moreover, this research aims to develop a highly precise stroke-onset prediction method by machine learning that integrates engineering information obtained by mechanical simulation with medical information. Specifically, a classifier predicting whether a cerebral aneurysm that causes subarachnoid hemorrhage would rupture was constructed via machine learning using medical data and CFD simulation data of cerebral blood flow as inputs. Factors that govern cerebral aneurysm rupture were also extracted.

The rest of the paper is organized as follows. In Section 2, we describe the data required to build the proposed classification model along with the process of training the classifier. Section 3 illustrates the results of model building as well as the discussion of the numerical experiments. We conclude the paper in Section 4.

2 METHODS

2.1 Dataset

The total of 6,470 cases had registered to the Jikei University's database, we first extracted cases for each location of occurrence of the aneurysm. If the case was unruptured, we then extracted the cases that are being observed and have not been treated in the past, and if the case was ruptured, we then extracted the cases that ruptured during follow-up visits. In addition, we used morphology to restrict the cases to those in which the length, width, and neck of the bulge are each less than 10 mm, but at least 1 of these measurement is greater than 3 mm. Furthermore, we restricted the unruptured cases to those in which the follow-up period[1] is over 2 years, and analyzed all consecutive cases that can be analyzed. In the end, the scope of this research was 338 cases.

The medical data and blood-flow-simulation data were collected from the 338 cases, 303 of which for unruptured and 35 for ruptured aneurysm samples.

2.1.1 Medical Data

There were two categories of the patients' medical history data used in the study. The first category is clinical information, including their age; gender; aneurysm location; history of subarachnoid hemorrhage (SAH); smoking; diabetes mellitus (DM); hypertension (HT); hyperlipidemia; alcohol consumption (Alcohol); polycystic kidneys (PK); cerebral hemorrhage (CH); hormone replacement (HR); and family history of SAH (FH_SAH), unruptured aneurysm (FH_Unruptured Aneurysm), PK (FH_PK). The other category is morphological information of cerebral aneurysm, including maximum aneurysm height, maximum neck diameter, neck area, volume, aspect ratio, side-wall or bifurcation type, and presence or absence of bleb. A total of 17 features were collected in the patients' medical data.

2.1.2 Blood-flow-simulation Data

Hemodynamic data were obtained through the CFD simulation of the cerebral blood flow. CFD is a branch of fluid mechanics that employs numerical analysis to solve problems that involve fluid flow. The simulation identified physical blood-flow characteristics such as PLC, EL, Energy Loss per Unit Volume (ELV), maximum WSS, average WSS, minimum WSS, and Oscillatory Shear Index (OSI), and the maximum, mini-

[1] The follow-up period is defined as the time between the initial consultation and the final consultation.

mum, amplitude, and average of these quantities were used in the study. Among these characteristics, PLC, EL and WSS were reported as helpful in predicting whether cerebral aneurysm would rupture (Shojima et al., 2004),(Qian et al., 2011),(Takao et al., 2012). A total of 53 features were collected in the blood-flow-simulation data.

The calculation conditions are summarized as follows. A prototype CFD solver (Siemens Healthcare GmbH, Forchheim, Germany, "Not to be used for Diagnosis and/or Therapy"), which utilizes the Lattice Boltzmann method, was used. With regards to the physical properties of blood, fixed density and viscosity values were set, and non-Newtonian fluids were disregarded. After considering a laminar flow field, the two pulses were calculated using the pulse conditions, and only results from the second pulse were used. The outlet boundary condition was set to an average static pressure of 0 Pa, and the calculations were established in a structured computational grid with a maximum size of 0.1 mm. For further details, see previous works (Qian et al., 2011),(Takao et al., 2012).

2.2 Classification Model for Cerebral Aneurysm Rupture Prediction

2.2.1 Oversampling of Minority Sample

The number of patients who suffer from ruptured aneurysm is far less than those who suffer from unruptured aneurysms, i.e., a classical class imbalance problem exists. Therefore, the synthetic minority oversampling technique (SMOTE) (Chawla et al., 2002) was ideal in generating the simulated instances for the classification model. As one of the powerful and effective approaches in various fields, SMOTE oversamples the minority class by taking each instance and introducing synthetic instances along the line segments joining any or all of the K-nearest neighbors in the minority class. A synthetic instance of an instance under consideration (called the base instance) is generated by first taking the difference between the feature vector of the base instance and its nearest neighbor, multiplying this difference by a random number between 0 and 1, and finally adding the product to the feature vector of the base instance. SMOTE was applied in this research to enlarge the number of samples with ruptured aneurysm.

2.2.2 Feature Selection

This study employed the SelectKBest algorithm for the selection of the useful features out of the 70 combined medical and blood-flow-simulation data features to serve as input for the classification model. SelectKBest uses a function (in this case f_classif, but could be others) to score the features and then removes all but those with the K highest scores.

2.2.3 Building a Classifier

The data sample is divided into training, verification, and test data while maintaining the ratio between the number of ruptured and unruptured samples. Here, the ratio of training data, verification data, and test data was set to 4:3:3. The training data was used to optimize the hyper parameter of the classification model using a grid search with stratified five-fold cross validation. On the other hand, the verification data was used to determine the optimum number and item of features. For $K = 1, \ldots, 70 (= 17 + 53)$, features were selected by the SelectKBest algorithm, their performance on the verification data was evaluated, and the optimum number of features and items were determined. Moreover, the test data were used to evaluate the final classification performance. Here, logistic regression and SVM were used as classifiers, and the performance of both methods were subsequently compared.

3 RESULTS AND DISCUSSION

3.1 Feature Selection

Results of the feature selections are organized in Tables 1 and 2. Approximately 40% of the features extracted as important features were medical data that doctors have used as judgment materials for diagnosis until now such as age and size of cerebral aneurysms. In contrast, the remaining 60% were cerebral blood-flow CFD simulation data such as WSS and PLC.

Table 1: Features selected: logistic regression.

Data Type	Description
Clinical information	Age, Aneurysm location, Multi/Single aneurysm
Morphological information	Max. height, Volume, Aspect ratio, Bleb
Hemodynamic information	Temporal max. spatial min. WSS, Temporal ave. spatial min. WSS, Temporal max. LSA, LSI, SCI, Temporal max. & ave. SCI, Temporal min. & ave. PLC
Total number of features	16

Table 2: Features selected: SVM.

Data Type	Description
Clinical information	Age, Aneurysm location, Multi/Single aneurysm, HT, HL
Morphological information	Side/Bifurcation, Max. height, Volume, Aspect ratio, Bleb
Hemodynamic information	Temporal max. spatial ave.WSS, Temporal max. spatial min WSS, Temporal min. spatial ave. WSS, Temporal min. spatial min.WSS, Temporal max LSA, LSI, SCI, Temporal ave. spatial ave. WSS, Temporal ave. spatial min.WSS, Temporal ave. spatial min. WSS, Temporal ave. PLC, SCI, Temporal min. LSI, PLC
Total number of features	27

3.2 Cerebral Aneurysm Rupture Prediction

The measures to evaluate the classification model were sensitivity, specificity, and F-measure.

Sensitivity, computed by Eq. (1), represents the fraction of actual correctly predicted ruptured samples from the total number of ruptured samples.

$$\text{Sensitivity} = \frac{\text{TruePositive}}{\text{TruePositive} + \text{FalseNegative}} \quad (1)$$

Specificity, computed by Eq. (2), represents the fraction of actual correctly predicted unruptured samples from the total number of unruptured samples.

$$\text{Specificity} = \frac{\text{TrueNegative}}{\text{TrueNegative} + \text{FalsePositive}} \quad (2)$$

F-measure is the harmonic mean of Precision and Sensitivity computed by Eq.(3).

$$\text{F-measure} = \frac{2\ \text{TruePositive}}{2\ \text{TruePositive} + \text{FalsePositive} + \text{FalseNegative}} \quad (3)$$

Tables 3 and 4 show the confusion matrix obtained by logistic regression and SVM, respectively. Table 5 summarizes the performance measures resulting from the test data classification by the two models.

Based on the performance measures of the two classifiers, logistic regression and SVM, logistic regression was found to slightly lower the specificity but greatly increase the sensitivity. In other words, using logistic regression made the classification more stable.

Table 3: Confusion matrix: logistic regression.

N=102		Actual class	
		Rupture	Unrupture
Predicted class	Rupture	7	14
	Unrupture	4	77

Table 4: Confusion matrix: SVM.

N=102		Actual class	
		Rupture	Unrupture
Predicted class	Rupture	5	8
	Unrupture	6	83

Table 5: Performance measures resulting from test data classification by the two models.

	logistic regression	SVM
Sensitivity	0.636	0.455
Specificity	0.846	0.912
F-measure	0.437	0.417

4 CONCLUSIONS

A classifier constructed by machine learning using combined medical and cerebral blood-flow-simulation data was used for prediction of cerebral aneurysm rupture in a total of 338 cerebral aneurysm data samples (35 ruptured, 303 unruptured). SMOTE algorithm was used to resolve the imbalance of data, while SelectKBest algorithm was applied to the 70 features, resulting in the extraction of 27 important features. Among the features extracted, 40% belong to the medical data while 60% were from the blood-flow-simulation data. Using logistic regression as a classification model, we found the sensitivity of 0.64 and the specificity of 0.85. The results showed the possibility of highly accurate prediction of cerebral aneurysm rupture by machine learning using engineering information obtained from simulations.

Thus, this study successfully developed a classification model on stroke-onset prediction with data from three different sources. Although the number of cases used in the analysis was limited, the success and great performance of this model could still make a good reference for future research, even for doctors who could issue objective diagnoses by considering various data sources to help patients receive preventive treatment. Stroke detection and prevention could help more people and save medical resources, especially for an aging society like Japan.

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REFERENCES

Amini, L., Azarpazhouh, R., Farzadfar, M., Mousavi, S., Jazaieri, F., Khorvash, F., Norouzi, R., and Toghianfar, N. (2013). Prediction and control of stroke by data mining. *Int J Prev Med.*, 4(Suppl 2):S245–249.

Bentley, P., Ganesalingam, J., Jones, A., Mahady, K., Epton, S., Rinne, P., Sharma, P., Halse, O., Mehta, A., and Rueckert, D. (2014). Prediction of stroke thrombolysis outcome using ct brain machine learning. *Neuroimage Clin.*, 30(4):635–640.

Chawla, N., Bowyer, K., Hall, L., and Kegelmeyer, W. (2002). Smote: Synthetic minority over-sampling technique. *Journal of Artificial Intelligence Research*, 16:321–357.

Chung, B. and Cebral, J. (2015). Cfd for evaluation and treatment planning of aneurysms: review of proposed clinical uses and their challenges. *Ann Biomed Eng.*, 43(1):122–138.

Hitman, G., Colhoun, H., Newman, C., Szarek, M., Betteridge, D., Durrington, P., Fuller, J., Livingstone, S., Neil, H., and Investigators., C. (2007). Stroke prediction and stroke prevention with atorvastatin in the collaborative atorvastatin diabetes study (cards). *Diabet Med.*, 24(12):1313–1321.

Letham, B., Rudin, C., McCormick, T., and Madigan, D. (2015). Stroke prediction and stroke prevention with atorvastatin in the collaborative atorvastatin diabetes study (cards). *Annals of Applied Statistics*, 9(3):1350–1371.

Lumley, T., Kronmal, R., Cushman, M., Manolio, T., and Goldstein, S. (2002). A stroke prediction score in the elderly: validation and web-based application. *J Clin Epidemiol*, 55(2):129–136.

Manolio, T., Kronmal, R., Burke, G., O'Leary, D., and Price, T. (1996). Short-term predictors of incident stroke in older adults. *Stroke*, 27(9):1479–1486.

Morino, T., Tanoue, T., Tateshima, S., Vinuela, F., and Tanishita, K. (2010). Intra-aneurysmal blood flow based on patient-specific ct angiogram. *Experiments in Fluids*, 49(2):485–496.

Nogueira, R., Bor-Seng-Shu, E., Saeed, N., Teixeira, M., Panerai, R., and Robinson, T. (2016). Meta-analysis of vascular imaging features to predict outcome following intravenous rtpa for acute ischemic stroke. *Frontiers in Neurology*, 7(77):1–8.

Qian, Y., Takao, H., Umezu, M., and Murayama, Y. (2011). Risk analysis of unruptured aneurysms using computational fluid dynamics technology: preliminary results. *AJNR Am J Neuroradiol.*, 32(10):1948–1955.

Shojima, M., Oshima, M., Takagi, K., Torii, R., Hayakawa, M., Katada, K., Morita, A., and Kirino, T. (2004). Magnitude and role of wall shear stress on cerebral aneurysm: computational fluid dynamic study of 20 middle cerebral artery aneurysms. *Stroke*, 35(11):2500–2505.

Takao, H., Murayama, Y., Abe, T., Ishibashi, T., Yuki, I., Otsuka, S., Suzuki, T., Masuda, S., Mohamed, A., Sen, I., Yamamoto, M., and Abe, T. (2012). Cfd reveals hemodynamic differences between unruptured and ruptured intracranial aneurysms during observation. *Stroke*, 43(2):A2731.

Wang, T., Massaro, J., Levy, D., Vasan, R., Wolf, P., D'Agostino, R., Larson, M., Kannel, W., and Benjamin, E. (2003). A risk score for predicting stroke or death in individuals with new-onset atrial fibrillation in the community: the framingham heart study. *JAMA*, 290(8):1049–1056.

Xiang, J., Siddiqui, A., and Meng, H. (2014). The effect of inlet waveforms on computational hemodynamics of patient-specific intracranial aneurysms. *J Biomech.*, 47(16):3882–3890.