HJR
VOLUME 5 | ISSUE 4

ORIGINAL ARTICLE Neuro/Head and Neck Radiology

Development of an intelligent system for the determination of rupture-related characteristics in intracranial aneurysms detected by Computed Tomography Angiography

Petros Zampakis[1], Nontas Ntzanis[1], Vasilios Panagiotopoulos[2], Fotis Anagnostopoulos[1], Gerasimos A.T. Messaris[3], Christina Kalogeropoulou[1], Constantinos Koutsojannis[4]

[1]Department of Radiology, University Hospital of Patras, Greece
[2]Department of Neurosurgery, University Hospital of Patras, Greece
[3]Department of Medical Physics, University Hospital of Patras, Greece
[4]Department of Health Physics and Computational Intelligence, School of Health Rehabilitation Sciences, University of Patras, Greece

SUBMISSION: 29/4/2020 - ACCEPTANCE: 27/8/2020

ABSTRACT

Purpose: Aim of this study was the development of an intelligent system (IS) that can determine the rupture-related characteristics in intracranial aneurysms detected by computed tomography angiography.
Material and Methods: 100 intracranial aneurysms in 100 patients (74% ruptured) were analysed. An IS was developed based on machine learning (ML) algorithm (WEKA J48 software). The IS used measurements, morphological characteristics and location of the aneurysms, as well as patients' age. 70 aneurysms were used as the training set, while 30 aneurysms were used as the test set.
Results: Using training set, our model along with Neuroradiologist interaction indicated the following:

CORRESPONDING AUTHOR, GUARANTOR

Petros Zampakis
Department of Radiology, University Hospital of Patras, 26504 Patras, Greece,
Email: pzampakis@gmail.com

The two most important rupture-related aneurysmal characteristics were dome/neck ratio ≥1.96 and irregular shape (regardless of location). Other rupture-related characteristics included anterior circulation aneurysms that were irregular in shape (regardless of dimension) and posterior circulation aneurysms with maximum dimension ≤6.7 mm (regardless of shape). A negative-related characteristic for rupture included posterior circulation aneurysms with wide neck and maximum dimension >6.7 mm. The accuracy of the IS in our test set was 80%. Age did not influence aneurysmal risk status.

Conclusions: In the present study we developed an IS which, based on certain aneurysmal parameters, can accurately identify rupture-related characteristics. As a result of the interaction between ML algorithms and clinical expert, a number of rules were created that can be further evaluated in larger studies.

KEY WORDS

Intracranial aneurysm/risk factors; Rupture; CT angiography; Intracranial aneurysm; Rupture; Machine learning

Introduction

Non-traumatic subarachnoid haemorrhage (SAH), as a result of an intracranial aneurysm rupture, is a very serious and potentially life-threatening condition [1]. Given the fact that the prevalence of unruptured intracranial aneurysms (UIAs) is about 3% in the general population, it is important to manipulate patients harbouring a UIA, since a delicate balance between the natural history of the disease and complications from any possible treatment (endovascular or surgical) is evident [2, 3].

In the past, numerous risk factors for aneurysm rupture have been outlined, such as aneurysm size and location, irregular shape, neck-dome ratio, bottleneck factor, size ratio and height-to-width ratio [4-7], as well as wall shear stress (WSS) and other derivative haemodynamic factors [8-10]. Moreover, clinical risk scores for aneurysms rupture based on patient demographics and aneurysmal anatomical characteristics have been proposed to predict aneurysm risk rupture, but still the decision of treating such patients is challenging [11-13].

An intelligent system (IS) or expert system is a system with the ability to make decisions like those of an expert in a cognitive field. Expert systems are computer programs that are derived from a branch of computer science research called artificial intelligence (AI) [14, 15]. AI is a powerful computational process which may possibly describe, in a better way than statistical methods, random associations among several parameters in numerous medical databases. AI comprises many machine learning (ML) algorithms, i.e. data mining tools that are used for knowledge extraction from big data, dealing with well-described instances of a certain condition. The most popular way to represent knowledge in medicine are decision trees or production rules [16]. Some studies have shown the performance of specific ML algorithms for the prediction of aneurysmal risk rupture [17-22].

The present study aimed to develop an IS, based on morphological and topographic parameters derived from cerebral computed tomography angiographies (CTAs), that can determine rupture-related characteristics. The latter could be clinically useful when interpreting CTAs with UIAs or in patients presented with SAH and multiple aneurysms.

Material and Methods

This retrospective, single-center study was conducted at the tertiary Neurointerventional Center of our University Hospital, following the approval of the local Ethics Committee University Hospital of Patras research ethics board.

We retrospectively reviewed 100 cerebral CTAs (obtained from the database of our hospital) in 100 patients (33 male, 67 female) diagnosed with intracranial aneurysms, both ruptured and unruptured. Cases were proportionally selected based on the standard knowledge of intracranial aneurysmal frequency distribution and oth-

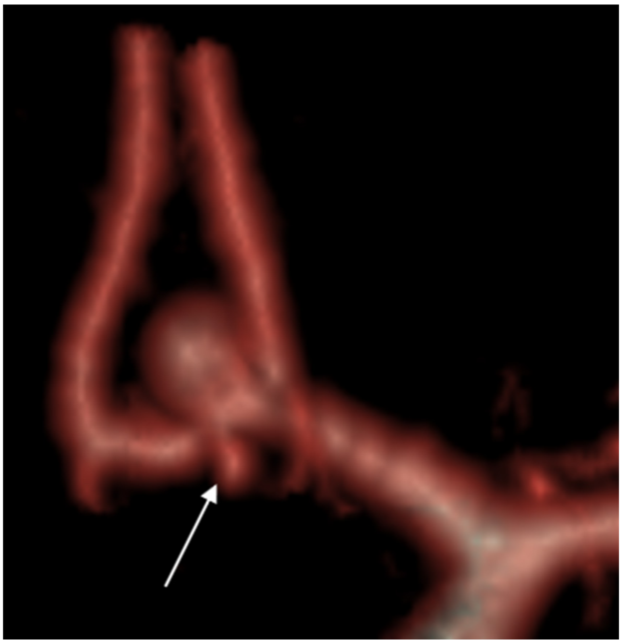

Fig 1. 3D reconstruction of computed tomography angiography shows an anterior communicating artery aneurysm. White arrow indicates irregularity of the aneurysmal sac (daughter sac).

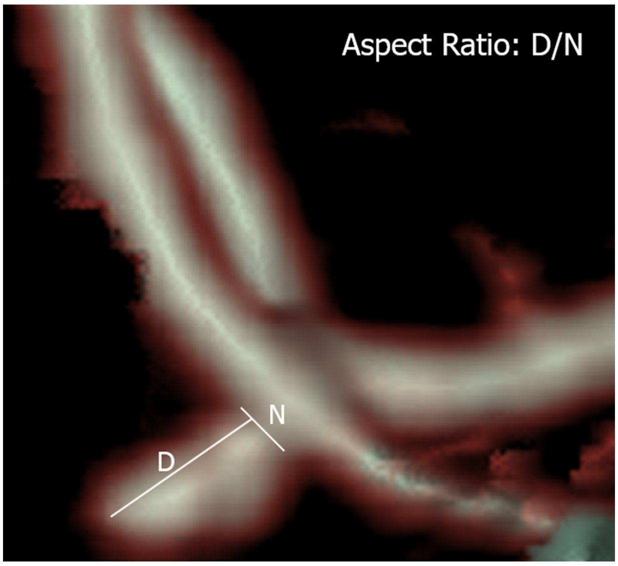

Fig 2. 3D reconstruction of computed tomography angiography shows an anterior communicating artery aneurysm with relatively high Dome/neck (ASPECT) ratio.

erwise in an unbiased and random manner. The mean age of patients was 57.34 ± 12 years (range between 22-82 years).

Cerebral CT Angiography

Cerebral CTA exams were performed on two CT systems (GE Lightspeed 16-slices GE Healthcare, USA and Toshiba Aquillion Prime 80 slices, Toshiba Corp, Japan). On both scanners, the protocol included a plain brain CT scan, followed by contrast-enhanced intracranial CTA, using a bolus tracking technique. Therefore, 60-80 ml of iodine agent depending on patient's cardiac status were used, at an injection rate of 4 ml/sec, with standard acquisition parameters.

Raw data were processed at dedicated workstations (Advantage WS-GE and VITREA respectively). The following morphologic characteristics of aneurysms were recorded and analysed:

A) aneurysm neck size in millimeters,

B) diameter vertical to the neck in millimeters,

C) the maximum dimension of the aneurysm in millimeters,

D) neck/dome ratio as well as dome/neck ratio (ASPECT ratio) and

E) regular or irregular shape (based on the presence of smooth rounded/oval shape or not, as well as the presence or not of a daughter sac) (**Fig. 1**).

Aneurysm dimensions were reliably measured on axial images or multiplanar reconstructions of 0.5 mm and 0.625 mm slices. In cases of complex morphology, a 3-D reconstruction of the aneurysm from the 0.5 mm and 0.625 mm slices of each CTA was used to guide measurement procedure (**Fig. 2**). Location of the aneurysms as well as anatomic variations of the circle of Willis were also recorded.

All morphological data were interpreted by an experienced neuroradiologist with >15 years of experience in intracranial CTAs. The patients' aneurysmal morphological data and their location are shown in **Table 1**.

Machine learning tools - Knowledge extraction from data (WEKA)

We applied the Waikato environment for knowledge analysis (WEKA), which is an open-source machine learning software platform, to extract knowledge by the form of rules. The software is readily available and can be downloaded from the official WEKA's site (https://www.cs.waikato.ac.nz/ml/weka/). It can be easily installed to all software platforms such as Windows, Mac OS, Linux etc. More

Table 1. Aneurysm parameters

Variable	Ruptured	Unruptured
Aneurysms	74 (74%)	26 (26%)
Neck/dome Ratio	0.51 ± 0.25	0.72 ± 0.31
Aspect Radio	1.96 ± 0.96	1.39 ± 0.59
Shape		
Regular	7 (7%)	6 (6%)
Irregular	67 (67%)	20 (20%)
Maximum Dimension (mm) 6.79 ± 4.12	6.79 ± 4.23	6.79 ± 3.88
Location		
AC (57%)	40 (40%)	17 (17%)
PC (43%)	34 (34%)	9 (9%)

specifically, a WEKA's J48 algorithm has been applied to approach our problem by creating a decision tree from our data. J48 is an algorithm used to generate decision trees [16].

Decision trees (which have the form of inverted tree) are the most popular way to represent knowledge, to extract interesting information or to build classification models and handling imbalanced data. They are built by partitioning the training dataset until the subsets contain only data belonging to a single class. When building a decision tree, the interaction with a human expert is crucial, by two important processes called pruning and attribute selection. By these processes, irrelevant and redundant attributes are being removed, thus improving accuracy of the model. Following decision tree build-up, the discovered knowledge is represented by the form of rules. Decision rules follow a general structure: If the conditions are met, then make a certain action. Finally, J48 creates a table named confusion matrix. Confusion matrix, or error matrix in many cases, has been used to describe the performance of a classification model (or "classifier") on a set of test data for which the output values are known [23-28].

Since machine learning algorithms have a mathematical basis and many directly incorporate statistics into their algorithms, we waived statistical analysis for our data set evaluation [29]. Our dataset comprised of 100 intracranial aneurysms and each one of them had the following attributes: patient's gender, patient's age, location of the aneurysm (Acom, Pcom, MCA, PCA, ICA, etc), maximum dimension, the aneurysm's shape, the neck/dome ratio, as well as the regional anatomic variations. Each one of them had also an output class named "RUPTURED" (YES or NO). The output class was known from the presence of SAH on plain CT or from the history of the patient.

Firstly, we used all attributes to create a decision tree, but we noticed that our model was very complex and confusing. Following attribute selection and pruning process, we ended up in the following: Aneurysms were divided into anterior or posterior circulation (AC, PC) while regional anatomic variations were excluded since they were apparent only in one anatomic location in our dataset. Although we know that patient's gender is an important epidemiologic characteristic and has been addressed as an independent risk factor for rupture, it had to be excluded from our study during attribute selection process. In fact, when patient's gender was initially included in our model, this proved to be very complex, confusing, and "noisy". This occurred because aneurysms were proportionally selected based on the standard knowledge of intracranial aneurysmal frequency distribution and not based on the gender of the patient.

Finally, we configured the dataset to contain the attributes age, location, maximum dimension, shape, ratio (neck) / (vertical neck) with RUPTURED output class. The new dataset was divided by the J48 algorithm into two subsets in a random way, a training set that was used to construct the decision tree and a test set that was used to evaluate its accuracy. The training set included 70 aneurysms and the remaining randomly divided dataset was the test set (30 aneurysms, 23 of them ruptured). We used four combinations of dataset attributes to achieve better classification results and during the process all created decision trees were tested for their reliability by the expert neuroradiologist, thus we ended up to the one that included: location (LOCI), maximum dimension (Dm), shape (Ir.Sh) and neck/dome ratio (**Fig. 3**).

Rules were generated as a result of our existing data analysis following a selection process (attribute selection and pruning) that combined neuroradiologist's expert knowledge, experience and existing literature, so that the rules would have a scientific basis.

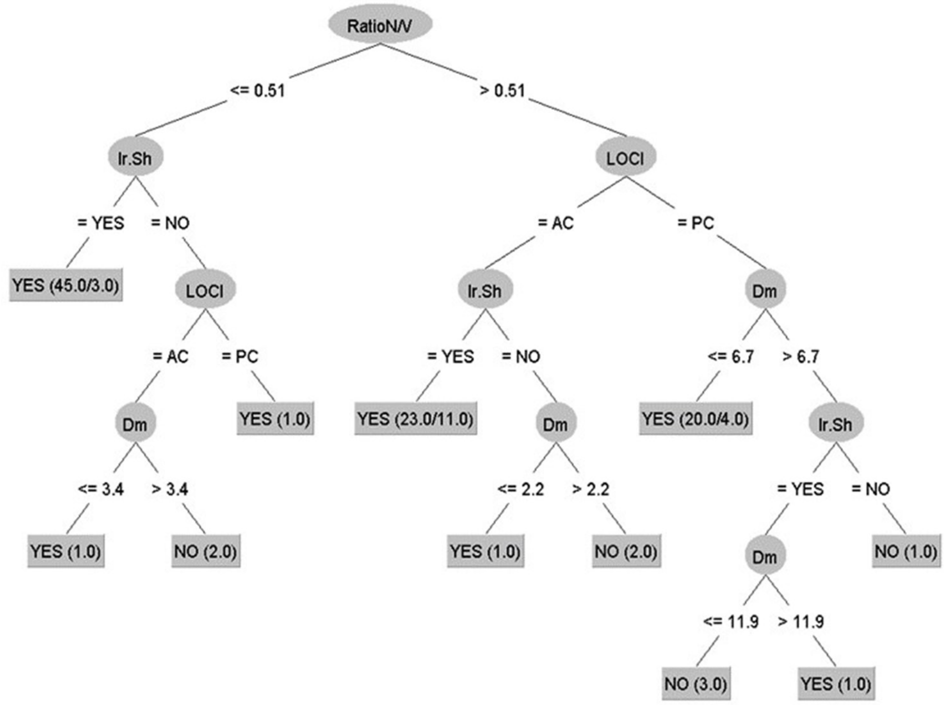

***Fig 3.** WEKA's J48 decision tree.*

Results

The interpretation of the created decision tree resulted in the following knowledge extraction:

1. The dominant attribute (root node) that influences the rupture status of the aneurysms of our dataset is dome/neck ratio (ASPECT ratio-AR) of 1.96 (or neck/dome ratio of 0.51).

2. The second most frequent parameter that influences the rupture status is the irregular shape.

3. Patient's age did not appear to influence our results.

Considering the generated decision rules, the following results were evident:

The two most important rupture-related aneurysmal characteristics were dome/neck ratio ≥1.96 and irregular shape (regardless of location). Other rupture-related characteristics included AC aneurysms that were irregular in shape (regardless of dimension) and posterior circulation aneurysms with maximum dimension ≤6.7 mm (regardless of shape). A negative-related characteristic for rupture included PC aneurysms with wide neck and maximum dimension >6.7 mm.

The overall rates for the created classification model based on decision tree algorithm were: Weighted Average Accuracy 80%, Precision 84.1%, Sensitivity 80%, Specificity 34%.

The created confusion matrix, describing the performance of our classification model is shown in **Table 2**. As it has been shown, 6 unruptured aneurysms of our test set were misclassified as ruptured (false-positive). A more detailed analysis of the decision tree showed that the feature, which was evident in all misclassified aneurysms, was an irregular shape, i.e. the model classified unruptured irregular shape aneurysms as ruptured.

Discussion

Based on the results of our detection model, the most dominant morphologic characteristic that correlates with rupture of an intracranial aneurysm (regardless of location and maximum dimension), is AR of 1.96 or Neck/dome ratio of 0.51. This finding is in keeping with the findings in current literature. Many theories have been postulated to explain why narrow-necked aneurysms are more vulnerable to rupture [30-33]. Several studies have also addressed the importance of this ratio, although this characteristic was not included as a risk factor in "International Study on Unruptured Intracranial Aneurysms" studies [34-36]. Even though the threshold of this parameter seems to vary amongst different studies (from 1.05 to 2.3) it has been reported that the higher the ASPECT ratio,

Table 2. Weka's J48 Confusion Matrix

Data class	A	B	‹‹‹‹ Classified as
Actual Positive	True-positive 23	False-negative 0	A=RUPTURED
Actual Negative	False-positive 6	True-negative 1	B=UNRUPTURED

the more likely the aneurysm is to rupture [8, 12, 13, 37, 38], although some aneurysms with relatively wide necks, in certain weather conditions will eventually rupture [39].

In our study the second most frequent parameter found to correlate with aneurysmal rupture (and a constant finding in anterior circulation) was the irregular shape of the aneurysm. Nevertheless, we believe that this feature is the most important, as it significantly influenced the accuracy of our study in a certain way. More specifically, a very low specificity was evident in the group of unruptured aneurysms, meaning that numerous of unruptured aneurysms were classified as ruptured. On the contrary, all ruptured aneurysms were correctly classified, thus the overall prediction accuracy for each class was high. The overall ability of our model to classify ruptured aneurysms was high as opposed to its ability to classify unruptured aneurysms. We found that false-positive instances (6 in total) related to unruptured aneurysms of our test set were classified as ruptured aneurysms. Based on the characteristics of our dataset, our model classified 6 out of 7 unruptured aneurysms as ruptured (**Table 2**). One could argue that this observation could be the result of the small imbalanced sample of the test set which mostly comprised of ruptured aneurysms, but on the other hand we know that decision trees frequently perform well on imbalanced data. Furthermore, a more detailed analysis of the decision tree which performed to explain our results showed that the feature that was evident in all misclassified aneurysms was an irregular shape, i.e. the model classified unruptured irregular shape aneurysms, as ruptured. This is quite important, as it highlights the importance of irregular shape in an unruptured aneurysm as a potential instability factor. Besides, it is well known that irregular shape is an important factor related to rupture. Many studies have highlighted the importance of this feature and revealed higher rates of rupture in aneurysms with irregular shape or daughter sac [6, 40-42]. It has been assumed that a weakness in the wall, or differences in wall shear stress within the aneurysmal sac, could be responsible for the rupture.

Although it is known that post-rupture morphology is not always the same with the pre-rupture model, in a large observational study by Lindgren et al. [40] it was found that a number of aneurysms had been ruptured during follow-up. In only 20% of them the shape had been changed.

An attractive hypothesis suggests that aneurysms grow over time, with periods of relative stability as well as potentially rapid growth, therefore harbouring a nonconstant risk of rupture over time. Consequently, the presence of irregularity in an unruptured aneurysm might well mean wall instability and potential increased risk of rupture, regardless of the size of the aneurysm [30, 43, 44].

Those two main morphologic characteristics that our model detected, as strong rupture-related factors (irregular shape and high AR), have been also addressed in other AI studies. Tanioka et al. [20] in a very recent study applied a Random Forest ML algorithm to morphologic and haemodynamic data of cerebral aneurysms (based on CTA images) and created three classification models to correctly identify the rupture status. The model consisting of only morphologic variables achieved overall accuracy of 77.0%, with the most important parameters being the relationship between neck and dome of the aneurysm and irregular shape, as in our study. Liu et al. extracted morphological features of 719 aneurysms, by using PyRadiomics and found that the most important factor for stability was flatness (i.e. smooth shape), while unstable aneurysms showed irregularity especially in patients with hypertension [19].

Two other interesting remarks of our study are related to posterior circulation aneurysms. These aneurysms are of great importance, because of their increased morbidity and mortality rates, as well as their higher rupture risk (when compared to anterior circulation). Regarding posterior circulation, our study showed that a rupture-related characteristic included maximum dimension ≤6.7 mm (regardless of shape), while a negative-related characteristic for rupture included wide neck and maximum dimension >6.7 mm.

Although these results partially contradict the results of the "International Study of Unruptured Intracranial Aneurysms" and other studies [4, 5, 45], they are in keeping with a very interesting study by Hostettler et al. [46], where most ruptured aneurysms were smaller than 10 mm. This might be explained by the hypothesis in which rapidly developing unstable aneurysms that eventually rupture are expected to be relatively small. So, larger incidentally discovered aneurysms of the posterior circulation are not in danger of rupture, because they have been stabilised, contrary to smaller aneurysms which might not have reached this critical stabilisation point.

Finally, the patients' age did not influence our results, although data from large observational studies has shown that younger age (<40 years) is an important factor that might influence the decision-making procedure to treat an unruptured aneurysm [47]. This was included in a recently proposed scoring system by Juvela [13].

Many efforts have been made to create classification tools to assess the risk of rupture of an unruptured aneurysm, based on AI algorithms. The current data literature shows heterogeneity, with implication of different AI tools, based on different angiographic modalities [18, 19]. Nevertheless, some studies showed similar results to our detection model, while others showed better performance. The latter used models that were complicated, multifactorial whereas methodological issues were evident [22]. For example Liu et al. studied 594 anterior communicating arteries aneurysms, by using artificial neural network, and achieved overall prediction accuracy of 94.8 % [17]. As de Jong highlighted, the above study had some methodological issues and such high accuracy rates should be dealt with caution, because "training an artificial neural network with a mix of real and synthetic data might lead to non-realistic prediction precision" [48]. Finally, some studies were not intended to determine and predict rupture-related characteristics but were used only for knowledge extraction [21].

Strengths of our study are the following: WEKA's J48 decision's tree rules are easily understandable to radiologists. Another advantage of our determination model is the interaction between the AI systems (machine) and the expert (human). It was due to this interaction that the decision trees were valid and came up with reasonable results. Another potential advantage of our study is that we chose to incorporate relatively simple model parameters, thus making our model easy to apply in everyday practice. By doing so, expert professionals might take advantage of it, without having to encompass any sophisticated data, other than aneurysm dimensions, morphology and topography. The aforementioned information is readily available from CTAs data, which is anyway performed in such patients.

Our study has certain limitations. We incorporated a relatively small sample of aneurysms, while the number of cases between ruptured and unruptured aneurysms was not balanced. A smaller number of patients with unruptured intracranial aneurysms were included, because most of our patients harboured ruptured aneurysms. Although AI tools are not entirely dependent on sample size, a larger study group is desirable. Moreover, decision trees frequently perform well on imbalanced data [49, 50], but such imbalance could underestimate the performance of the system. For example, in a larger sample of unruptured aneurysms with regular shape, these might have been classified correctly, thus our model could have shown higher accuracy. Furthermore, our results regarding the posterior circulation aneurysms, although interesting, were based on a small-sized sample of patients and do not represent an evidenced based fact. For ethical reasons, we did not perform a long-term follow-up study in unruptured aneurysms, so evolution before rupture as well as information about the morphology of aneurysms before and after rupture could not be recorded. Therefore, a large, prospective, multicenter study is needed to verify our findings in the future.

Future plans include improvements of system's accuracy, validation of the IS in a larger test set sample, as well as the creation of an application based on this algorithm, which can be used as a supportive or adjunctive tool of less experienced radiologists to highlight rupture-related factors.

Conclusions

In the present study, we developed an IS based on certain aneurysmal parameters that can determine rupture-related characteristics. Our system, because of the interaction between ML algorithms and clinical expert, created some new rules which can be further evaluated in larger studies. Its inability to correctly classify unruptured aneurysms reduces the overall success rate. However this discrepancy, associated with unruptured aneurysms of irregular shape, could point out that such aneurysms are at a higher risk of rupture. **R**

Abbreviations

Acom = anterior communicating artery
Pcom or Pcomm = posterior communicating artery
MCA = middle cerebral artery
PCA = posterior cerebral artery
ICA = internal carotid artery

Acknowledgements

The authors would like to thank Professor of Computer Engineering & Informatics Ioannis Hatzilygeroudis for his consultation and scientific support.

Funding

This project did not receive any specific funding.

Ethical approval

The study was approved by University Hospital of Patras Research Ethics Board (REB).

Conflict of interest

The authors declared no conflicts of interest.

References

1. Steiner T, Juvela S, Unterberg A, et al. European Stroke Organization. European Stroke Organization guidelines for the management of intracranial aneurysms and subarachnoid haemorrhage. *Cerebrovasc Dis* 2013; 5(2): 93-112.
2. Hackenberg KAM, Hänggi D, Etminan N. Unruptured intracranial aneurysms. *Stroke* 2018; 49(9): 2268-2275.
3. Thompson BG, Brown RD Jr, Amin-Hanjani S, et al. American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, and Council on Epidemiology and Prevention; American Heart Association; American Stroke Association. Guidelines for the management of patients with unruptured intracranial aneurysms: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2015; 46(8): 2368-2400.
4. International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms-risk of rupture and risks of surgical intervention. *N Engl J Med* 1998; (339): 1725-1733.
5. Wiebers DO, Whisnant JP, Huston J 3rd, et al. International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet* 2003; 362 (9378): 103-110.
6. UCAS Japan Investigators. Morita A, Kirino T, Hashi K, et al. The natural course of unruptured cerebral aneurysms in a Japanese cohort. *N Engl J Med* 2012; 366(26): 2474-2482.
7. Takao H, Murayama Y, Otsuka S, et al. Hemodynamic differences between unruptured and ruptured intracranial aneurysms during observation. *Stroke* 2012; 43(5): 1436-1439.
8. Xiang J, Natarajan SK, Tremmel M, et al. Hemodynamic–morphologic discriminants for intracranial aneurysm rupture. *Stroke* 2011; 42(1): 144-152.
9. Ren Y, Chen GZ, Liu Z, et al. Reproducibility of image-based computational models of intracranial aneurysm: a comparison between 3D rotational angiography, CT angiography and MR angiography. *Biomed Eng Online* 2016; 15(1): 50.
10. Riccardello GJ Jr, Shastri DN, Changa AR, et al. Influence of relative residence time on side-wall aneurysm inception. *Neurosurgery* 2018; 83(3): 574-581.
11. Greving JP, Wermer MJ, Brown RD Jr, et al. Development of the PHASES score for prediction of risk of rupture of intracranial aneurysms: a pooled analysis of six prospective cohort studies. *Lancet Neurol* 2014; 13(1): 59-66.
12. Etminan N, Brown RD Jr, Beseoglu K, et al. The unruptured intracranial aneurysm treatment score: a multidisciplinary consensus. *Neurology*

2015; 85(10): 881-889.
13. Juvela S. Treatment Scoring of Unruptured Intracranial Aneurysms. *Stroke* 2019; 50(9): 2344-2350.
14. Abu-Nasser SB. Medical Expert Systems Survey. International Journal of Engineering and Information Systems. 2017, 1 (7), pp.218-224.
15. Shortliffe EH. Medical expert systems--knowledge tools for physicians. *West J Med* 1986; 145(6): 830-839.
16. Kalogeropoulou C, Zampakis P, Tsimara M, et al. Intelligent System for preoperative evaluation of parathyroid gland for surgical intervention prediction. *J Clin Exp Radiol* 2019; 2(1).
17. Liu J, Chen Y, Lan L, et al. Prediction of rupture risk in anterior communicating artery aneurysms with a feed-forward artificial neural network. *Eur Radiol* 2018; 28(8): 3268-3275.
18. Kim HC, Rhim JK, Ahn JH, et al. Machine learning application for rupture risk assessment in small-sized intracranial aneurysm. *J Clin Med* 2019; 8(5): 683.
19. Liu Q, Jiang P, Jiang Y, et al. Prediction of aneurysm stability using a machine learning model based on PyRadiomics-derived morphological features. *Stroke* 2019; 50(9): 2314-2321.
20. Tanioka S, Ishida F, Yamamoto A, et al. Machine learning classification of cerebral aneurysm rupture status with morphologic variables and hemodynamic parameters. *Radiology* 2020: Artificial Intelligence. Published Online: Jan 15 2020. https://doi.org/10.1148/ryai.2019190077.
21. Silva MA, Patel J, Kavouridis V, et al. Machine learning models can detect aneurysm rupture and identify clinical features associated with rupture. *World Neurosurg* 2019; 131: e46-e51.
22. Bisbal J, Engelbrecht G, Villa-Uriol MC, et al. Prediction of cerebral aneurysm rupture using hemodynamic, morphologic and clinical features: A data mining approach. Database and Expert Systems Applications: 22nd International Conference, DEXA 2011, Toulouse, France, August 29 - September 2, 2011, Proceedings, Part II (pp.59-73) DOI: 10.1007/978-3-642-23091-2_6.
23. Karabadji NE, Seridi-Bouchelaghem H, Khelf I, et al. Improved decision tree construction based on attribute selection and data sampling for fault diagnosis in rotating machines. *Eng Appl Artif Intell* 2014; 35: 71-83.
24. Lima C, de Assis F, Souza C. An empirical investigation of attribute selection techniques based on Shannon, Rényi and Tsallis entropies for network intrusion detection. *Am J Intell Syst* 2012; (2): 111-117.
25. Dietterich TG. Overfitting and undercomputing in machine learning. *ACM Comput Surv* 1995; 27: 326-327.
26. Hawkins DM. The problem of overfitting. *J Chem Inf Comput Sci* 2004; 44(1): 1-12.
27. Stehman S. Selecting and interpreting measures of thematic classification accuracy. *Remote Sens Environ* 1997; (62): 77-89.
28. Tharwat A. Classification assessment methods. Appl Comput Inform 2018; https://doi.org/10.1016/j.aci.2018.08.003.
29. Cunningham SJ. Machine Learning and Statistics: A Matter of Perspective. New Zealand J Computing. 1995, 6 (1a), pp. 69–73.
30. Nader-Sepahi A, Casimiro M, Sen J, et al. Is aspect ratio a reliable predictor of intracranial aneurysm rupture? *Neurosurgery* 2004; 54: 1343-1348.
31. Tateshima S, Chien A, Sayre J, et al. The effect of aneurysm geometry on the intra-aneurysmal flow condition. *Neuroradiology* 2010; 52: 1135-1141.
32. Feigin VL, Anderson CS, Rodgers A, et al. Subarachnoid haemorrhage occurrence exhibits a temporal pattern—evidence from meta-analysis. *Eur J Neurol* 2002; 9: 511-516.
33. Bhogal P, AlMatter M, Hellstern V, et al. Difference in aneurysm characteristics between ruptured and unruptured aneurysms in patients with multiple intracranial aneurysms. *Surg Neurol Int* 2018; 9: 1.
34. Kleinloog R, de Mul N, Verweij BH, et al. Risk factors for intracranial aneurysm rupture: A systematic review. *Neurosurgery* 2018; 82(4): 431-440.
35. Liu Q, Jiang P, Wu J, et al. Intracranial aneurysm rupture score may correlate to the risk of rebleeding before treatment of ruptured intracranial aneurysms. *Neurol Sci* 2019; 40(8): 1683-1693.

36. Ujiie H, Tamano Y, Sasaki K, et al. Is the aspect ratio a reliable index for predicting the rupture of a saccular aneurysm? *Neurosurgery* 2001; 48: 495-503.
37. Dhar S, Tremmel M, Mocco J, et al. Morphology parameters for intracranial aneurysm rupture risk assessment. *Neurosurgery* 2008; 63: 185-196, discussion: 196-187.
38. Ghosh S, Dey S, Tjoumakaris S, et al. Association of morphologic and demographic features of intracranial aneurysms with their rupture: a retrospective analysis. *Acta Neurochir* 2013; Suppl 115: 275-278.
39. Li M, Hu S, Yu N, et al. Association between meteorological factors and the rupture of intracranial aneurysms. *J Am Heart Assoc* 2019; 8(17): e012205.
40. Lindgren AE, Koivisto T, Björkman J, et al. Irregular shape of intracranial aneurysm indicates rupture risk irrespective of size in a population-based cohort. *Stroke* 2016; 47(5): 1219-1226.
41. Björkman J, Frösen J, Tähtinen O, et al. Irregular shape identifies ruptured intracranial aneurysm in subarachnoid hemorrhage patients with multiple aneurysms. *Stroke* 2017; 48(7): 1986-1989.
42. Abboud T, Rustom J, Bester M, et al. Morphology of ruptured and unruptured intracranial aneurysms. *World Neurosurg* 2017; 99: 610-617.
43. Brinjikji W, Zhu YQ, Lanzino G, et al. Risk factors for growth of intracranial aneurysms: A systematic review and meta-analysis. *AJNR Am J Neuroradiol* 2016; 37: 615-620.
44. Skodvin TØ, Johnsen LH, Gjertsen Ø, et al. Cerebral aneurysm morphology before and after rupture: Nationwide case series of 29 aneurysms. *Stroke* 2017; 48: 880-886.
45. Huhtakangas J, Lehecka M, Lehto H, et al. CTA analysis and assessment of morphological factors related to rupture in 413 posterior communicating artery aneurysms. *Acta Neurochir (Wien)* 2017; 159(9): 1643-1652.
46. Hostettler IC, Alg VS, Shahi N, et al. Genetics and Observational Subarachnoid Haemorrhage (GOSH) study investigators. Characteristics of unruptured compared to ruptured intracranial aneurysms: A multicenter case-control study. *Neurosurgery* 2018; 83(1): 43-52.
47. Waqas M, Rajabzadeh-Oghaz H, Tutino VM, et al. Morphologic parameters and location associated with rupture status of intracranial aneurysms in elderly patients. *World Neurosurg* 2019; 129: e831-e837.
48. de Jong GA, Aquarius R. Use of artificial neural networks to predict anterior communicating artery aneurysm rupture: possible methodological considerations. *Eur Radiol* 2019; 29(5): 2724-2726.
49. Truică CO, Leordeanu C. Classication of an imbalanced data set using decision tree algorithms. *UPB Sci Bull Ser C* 2017; 79: 69-84.
50. Ramyachitra D, Manikandan P. Imbalanced dataset classification and solutions: A review. *Int J Bus Res* 2014; 5: 4.

READY - MADE CITATION

Zampakis P, Ntzanis N, Panagiotopoulos V, Anagnostopoulos F, Messaris G.A.T., Kalogeropoulou C, Koutsojannis C. Development of an intelligent system for the determination of rupture-related characteristics in intracranial aneurysms detected by Computed Tomography Angiography. *Hell J Radiol 2020*; 5(4): 8-17.