The severity of the clinical signs and symptoms of cranial dural arteriovenous fistulas (DAVFs) is well correlated with their pattern of venous drainage. Although the presence of cortical venous drainage can be considered a potential predictor of aggressive DAVF behaviors, such as intracranial hemorrhage or progressive neurological deficits due to venous congestion, accurate statistical analyses are currently not available. Using a decision tree data mining method, the authors aimed at clarifying the predictability of the future development of aggressive behaviors of DAVF and at identifying the main causative factors.

METHODS Of 266 DAVF patients, 89 were eligible for analysis. Under observational management, 51 patients presented with intracranial hemorrhage/infarction during the follow-up period.

RESULTS The authors created a decision tree able to assess the risk for the development of aggressive DAVF behavior. Evaluated by 10-fold cross-validation, the decision tree's accuracy, sensitivity, and specificity were 85.28%, 88.33%, and 80.83%, respectively. The tree shows that the main factor in symptomatic patients was the presence of cortical venous drainage. In its absence, the lesion location determined the risk of a DAVF developing aggressive behavior.

CONCLUSIONS Decision tree analysis accurately predicts the future development of aggressive DAVF behavior.

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KEY WORDS predictability; decision tree analysis; dural arteriovenous fistulas; vascular disorders

The severity of the clinical signs and symptoms of cranial dural arteriovenous fistulas (DAVFs) is correlated with their pattern of venous drainage and the location of the lesions. Among angiographic findings, cortical venous drainage rather than occlusion of the venous sinus or retrograde flow in the arteriovenous shunt is considered the strongest factor implicated in an aggressive clinical presentation and includes intracranial hemorrhage and progressive neurological deficits due to venous congestion. The propensity for cortical venous drainage depends on the lesion location. Fistulas in the anterior cranial fossa or tentorial notch tend to manifest cortical venous drainage and an aggressive neurological course once they produce symptoms and signs. Cavernous sinus DAVFs usually present with mild symptoms, such as tinnitus and chemosis, because they are less likely to involve cortical venous drainage. Although the presence of cortical venous drainage can be considered a potential predictor of an aggressive clinical course, accurate statistical analyses of factors that can influence the disease prognosis are not currently available. In this study we aimed at elucidating the predictability of the future development of aggressive DAVF behaviors, such as intracranial hemorrhage and the progression of neurological deficits, including cerebral infarction due to venous congestion from a multifactorial perspective. We also attempted to identify the main factors...
influencing the risk for aggressive conversion in the order of significance using the decision tree analysis\textsuperscript{12} used in data mining.

Decision trees are powerful prediction methods that have been used successfully in different areas of medicine.\textsuperscript{11} Choi et al.\textsuperscript{3} developed a decision tree for patients with severe head injury. Andrews et al.,\textsuperscript{1} who compared classic logistic regression and decision tree analyses for predicting recovery in patients with traumatic brain injury, showed that decision trees yielded more information. In contrast to classic statistical methods that assume that factors exert the same effect over the entire data set, decision trees recursively divide data into subgroups and investigate the effects of different factors based on their statistical importance for different subgroups.

**Methods**

Of 266 DAVF patients, we considered 89 conservatively treated patients to be eligible for this study. The remaining 177 patients were excluded to eliminate treating-physician bias; patients who had received any surgical or endovascular treatment were excluded. Of the 89 included patients, 39 presented with transverse/sigmoid sinus, 22 with cavernous sinus, 11 with anterior cranial fossa, 7 with tentorial, 6 with superior sigmoid sinus, and 3 with hypoglossal canal lesions, and 1 with a craniofacial junction lesion; 16 patients were diagnosed incidentally.

During follow-up, DAVFs in 51 of the 89 patients (57.3%) demonstrated aggressive behavior, including intracranial hemorrhage, and progressive neurological deficits, including cerebral infarction due to venous congestion. The average interval between presenting with mild symptoms or incidental diagnosis and aggressive conversion was 4 months (range 7 days to 41 months) clinically and 5 months (range 10 days to 43 months) radiographically. Of the 51 patients harboring DAVFs with aggressive behavior, 35 presented with intracranial hemorrhage (intracerebral hemorrhage [ICH] in 16; subarachnoid hemorrhage [SAH] in 5; intraventricular hemorrhage [IVH] in 1; ICH and SAH in 3; ICH and IVH in 5; ICH and subdural hematoma in 4; and ICH, SAH, and IVH, in 1). The remaining 16 patients had progressive neurological deficits due to venous congestion.

For our study we selected factors reported to influence the natural history of DAVFs.\textsuperscript{2,10} Patient age and sex, lesion location, cortical venous drainage, absence of symptoms (incidental diagnosis), presence of symptoms/signs (consciousness disturbance, headache, convulsion, tinnitus, vomiting, blepharoptosis, eye pain, chemosis, exophthalmos, diplopia, dementia, dizziness/vertigo, and hydrocephalus), medical history (hypercoagulopathy, previous surgery, head injury, and chronic disease), and the multiplicity of DAVF were used as inputs into the decision tree model to predict the future development of aggressive DAVF behavior.

The tree was generated using a combination of feature selection procedures\textsuperscript{4} and the C4.5 decision tree algorithm (J. Ross Quinlan C4.5: Programs for Machine Learning Morgan Kaufmann Series in Machine Learning) using RapidMiner 5.3 software (RapidMiner Inc., http://www.rapidminer.com). Decision trees are classification methods widely used in data mining because they are visually informative. A decision tree is generated by recursively splitting the patients according to the values of a statistically important factor. The statistical importance of each factor is evaluated with the C4.5 algorithm using the entropy function applied in information theory. Factors with high entropy reduction are considered of statistical importance. First, the most important factor for all patients is selected, and the patients are divided into subgroups based on the selected factor. For example, if the lesion location is the selected factor, each lesion location results in a subgroup. The procedure is then repeated, and each subgroup is divided again based on its most important factor until all patients in a specific subgroup are in the same class or the subgroup is no longer subject to further splitting. In data mining, the group that contains all patients is the root, each subgroup is a node, and the subgroups not subject to further division are the leaves. The leaves embody the final decision. Using the recorded factors of a new patient, risk can be predicted by following the decision tree path from the root to a node to one of the leaves.

For decision tree accuracy, it is important that the tree provide accurate results not only with respect to existing cases but also to new cases. One method for estimating the performance of the decision tree with new cases is to test the tree by using a test case that is different from the same population. However, in this approach the calculated performance is highly dependent on the selected test case. To overcome the effect of this dependency, we used 10-fold cross-validation to estimate the decision tree accuracy, sensitivity, and specificity. We randomly divided the existing data into 10 equally sized subsets and used each of the 10 subsets once as a testing set. The remaining 9 subsets were used for generating a decision tree. Finally, the overall accuracy, sensitivity, and specificity of the decision tree were calculated as the average of its performance with the 10 test sets.

**Results**

Creation of the decision tree to assess the risk for developing intracranial hemorrhage/infarction involved a combination of feature selection procedures and the C4.5 decision tree algorithm (Fig. 1). The resulting tree yielded a mean (± SD) accuracy, sensitivity, and specificity of 85.28% ± 10.25%, 88.33% ± 13.10%, and 80.83% ± 17.10%, respectively, upon 10-fold cross-validation. The absence of symptoms (incidental diagnosis), cortical venous drainage, lesion location, chemosis, and tinnitus were factors used to predict aggressive conversion risks.

The most important factor was the absence of symptoms. Only 1 patient in whom the lesion was incidentally identified was at risk for developing intracranial hemorrhage/infarction; the remaining 15 patients were not at risk. Further investigation revealed cortical venous drainage in the at-risk patient. Seventy-three patients were diagnosed nonincidentally. Of these patients, 33 (45.21%) presented with cortical venous drainage, in 32 of whom (96.97%) aggressive DAVF behavior developed. In patients without cortical venous drainage (n = 40), the lesion
location determined the risk for the development of aggressive DAVF behavior. Three patients with hypoglossal canal lesions were at low risk for aggressive DAVF behavior; none suffered hemorrhage or infarction. All 3 patients with tentorial lesions were at risk and all developed aggressive DAVF behavior.

Among patients with transverse/sigmoid sinus lesions, patients suffering tinnitus mostly had a benign clinical course (5 of 6 patients). The absence of tinnitus was a potential risk for aggressive conversion (7 of 9 patients developed aggressive DAVF behavior).

In the group with cavernous sinus lesions, the absence of chemosis indicated a low risk for developing aggressive DAVF behavior (n = 4), while the presence of chemosis alerted to a high risk for developing aggressive behavior, especially when tinnitus was present (n = 2). The absence of tinnitus in patients with cavernous sinus lesions reduced their risk (8 of 13 patients were did not have hemorrhage/infarction).

**Discussion**

The natural history and clinical course of DAVFs are strongly influenced by existing venous drainage patterns. Cortical venous drainage detected angiographically predicts an aggressive neurological course, including intracranial bleeding and cerebral venous infarction due to venous congestion. Elsewhere, we reported that the natural history of DAVFs without cortical venous drainage was benign in 98.5% of patients and that 2% of patients were at risk for conversion of the lesion into an aggressive DAVF. Shah et al. reported that the annual rate of conversion to a higher-grade DAVF with cortical venous drainage was 1.0%; however, the annual rate of intracranial hemorrhage, nonhemorrhagic neurological deficits (NHDs), and DAVF-related death was 0%. On the other hand, the natural history of DAVFs with cortical venous drainage is worse. Van Dijk et al. reported that the annual mortality rate of patients with DAVFs with cortical venous drainage
was 10.4% and the annual morbidity rate of patients suffering CNS-related adverse events was 15% (intracranial hemorrhage 8.1%, nonhemorrhagic CNS deficits 6.9%). Duffau et al. found that DAVFs with cortical venous drainage are associated with a high risk for early rebleeding (35% within 2 weeks after the first hemorrhage) and that the consequences of subsequent hemorrhages are graver. According to Bulters et al., among DAVF patients with cortical venous drainage, those with venous ectasia presented with a 7-fold increase in the incidence of hemorrhage (3.5% without and 27% with ectasia).

In addition to angiographic findings such as cortical venous drainage with or without venous ectasia, the symptomatology at presentation can influence the natural history of the disease and its course. Söderman et al. reported that in patients with intracranial hemorrhage the annual risk for subsequent hemorrhage is approximately 7.4%, while in patients free of hemorrhage at presentation the risk for bleeding is approximately 1.5%. They concluded that the risks for developing neurological symptoms unrelated to hemorrhage are lower than previously reported.

In Borden Type III DAVFs, the dural arterial supply drains into the venous sinus, and high pressure in the sinus results in both anterograde and retrograde drainage via subarachnoid veins. Gross and Du compared the incidence of hemorrhage in DAVF patients presenting with and without hemorrhage, in DAVF patients with NHNDs, and in patients with Borden Type III DAVFs. They found that DAVFs with hemorrhagic presentation demonstrated a trend toward greater bleeding rates.

Strom et al. reported that among DAVF patients with cortical venous drainage, those with intracranial hemorrhage and NHNDs were more likely to experience adverse events than asymptomatic patients (19.0% vs 1.4%). Zipfel et al. found that the annual rate of intracerebral hemorrhage was 7.4%–7.6% in patients with and 1.4%–1.5% in patients without symptomatic cortical venous drainage. In terms of lesion location, fistulas in the anterior cranial fossa or tentorial notch tend to manifest cortical venous drainage and an aggressive neurological course once they produce symptoms and signs; however, the natural history of such incidentally diagnosed lesions was unclear. It remains to be determined how clinical symptoms correlated with cortical venous drainage affect the incidence of intracranial hemorrhage/infarction. Also, the significant order in which individual factors, such as symptomatology, angiographic findings, and lesion location, influence the disease course is yet to be elucidated.

Compared with other statistical analyses, decision trees create a map between input factors and output classes, and the mapping is learned automatically from available data. By avoiding the parametric approach and by not making assumptions based on input data, decision trees are well suited for analyzing nonlinear events. In addition, decision trees assess different factors for different patient subgroups; this is not possible with classic statistical methods. An important feature of decision trees is that, in addition to yielding a highly accurate final prediction, they provide easily interpreted outputs that explain how the prediction was reached. Therefore, they enable the expert to understand and accept or reject the final prediction.

This is the first study of DAVFs that demonstrates factors associated with an aggressive presentation at different levels of significance using decision trees. Because decision trees consider the symptomatology and known lesion location, their use may add to information gained through angiographic, CT, and MRI studies. The generated decision tree model has been evaluated using 10-fold cross-validation. For small data sets, Braga-Neto and Dougherty showed that cross-validation provides a low bias error estimator; however, it exhibits high variance. As a limitation of our study, we acknowledge that some leaves, such as some lesion location, contain only a small number of cases. We are in the process of collecting additional data to better understand particular situations.

Conclusions

Decision tree analysis used in data mining identified factors associated at different levels of significance (symptomatology > cortical venous drainage > lesion location) with an aggressive presentation in patients with DAVF. These factors can help to predict the future development of intracranial hemorrhage/infarction in DAVF patients.

References


Author Contributions
Conception and design: Satomi. Acquisition of data: Satomi. Analysis and interpretation of data: Satomi, Ghaibeh. Drafting the article: Satomi, Ghaibeh. Critically revising the article: Satomi, Ghaibeh. Reviewed submitted version of manuscript: Satomi, Moriguchi. Approved the final version of the manuscript on behalf of all authors: Satomi. Statistical analysis: Ghaibeh. Administrative/technical/material support: Satomi. Study supervision: Nagahiro.

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