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Can We Predict Poor Outcome in Stroke Patients Without Imaging Data? A Decision Tree Analysis of Stroke Patients

İnmede Kötü Prognozu Görüntüleme Yapmadan Tahmin Edebilir miyiz? İnmeli Hastalarda Karar Ağacı Analizi

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Abstract

Objective: The aging world population and increased cardiovascular risk factors contribute to stroke and stroke related morbidity. In this study, we aimed to analyze predictors of increased morbidity of ischemic stroke patients in a single stroke unit.

Materials and Methods: Stroke patients recorded in the Istanbul University Stroke Registry between 2014 and 2020 were included and decision tree analyses [chi-squared automatic interaction detection (CHAID) method] were conducted. Gender, diabetes, hypertension, previous stroke, ischemic heart disease, hyperlipidemia, diagnosis of pneumonia during hospitalization in the stroke unit, and atrial fibrillation were determined as possible indicators for poor clinical outcomes.

Results: We included 881 patients with ischemic stroke in the study according to the inclusion and exclusion criteria. The mean age of patients was 66.5±14.4 years and 59% of the patients were male. CHAID analysis revealed that the most important factor for predicting modified Rankin Scale (mRS) score >3 is pneumonia. In patients with mRS score >3 and without pneumonia; hypertension and hyperlipidemia were found to be risk factors for poor functional outcome.

Conclusion: Preventative measures in stroke patients should not be limited to secondary prophylaxis of stroke. Avoiding infections in the acute phase plays an essential role in achieving favorable clinical outcomes.

Keywords: Ischemic stroke, decision tree, CHAID, prognosis, stroke registry

Öz

Amaç: Yaşlanan dünya nüfusu ve artan kardiyovasküler risk faktörleri nedeniyle inme sıklığı ve inmeye bağlı morbidite giderek artmaktadır. Bu çalışmada, inme ünitemizdeki iskemik inmeli hastalarda morbidite oranlarını yükselten belirleyicilerin analizi amaçlanmıştır.

Gereç ve Yöntem: İstanbul Üniversitesi İnme Veri Bankası'na 2014-2020 yılları arasında kaydedilmiş iskemik inmeli hastalar çalışmaya dahil edilmiştir. Cinsiyet, diyabet, hipertansiyon, geçirilmiş inme öyküsü, iskemik kalp hastalığı, hiperlipidemi, inme ünitesinde yatış sırasında pnömoni tanısı ve atriyal fibrilasyon, kötü klinik sonlanımın olası göstergeleri olarak belirlenmiştir ve karar ağacı analizi (CHAID) yöntemi uygulanmıştır.

Bulgular: Çalışmaya dahil etme ve çalışmadan dışlama kriterlerine göre iskemik inme tanısı alan 881 hasta dahil edilmiştir. İskemik inmeli hastaların yaş ortalamaları 66,5±14,4 yıl idi ve hastaların %59'u erkekti. CHAID analizi ile pnömoninin modifiye Rankin Skalası (mRS) skoru >3 olan hastalarda en sık görülen risk faktörü olduğu ortaya konmuştur. Pnömonisi olmayan ve mRS skoru 3'ün üzerinde olan hastalarda ise hipertansiyon ve hiperlipidemi kötü prognoz için risk faktörleri olarak ortaya çıkmaktadır.

Sonuç: İnmeli hastalarda önleyici tedbirler sadece ikincil profilaksi ile sınırlı kalmamalıdır. İnmenin akut döneminde hastane enfeksiyonlarının önlenmesi iyi klinik sonlanım ile ilişkilidir.

Anahtar Kelimeler: İskemik inme, karar ağacı, CHAID, prognoz, inme veri bankası

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Introduction

Ischemic stroke (IS) is still one of the leading causes of mortality and morbidity worldwide (1). The aging world population and increased cardiovascular risk factors contribute to the stroke burden. Recent acute treatment options such as thrombolysis and thrombectomy have started to change the course of the disease (2). Nevertheless, the number of patients who are not suitable candidates for acute treatments and those who cannot receive acute treatment due to logistic issues cannot be underestimated even in the 21st century. The optimal secondary prophylaxis and diligent hospital care were shown to reduce mortality and morbidity, especially in stroke units (3). Not only appropriate antithrombotic treatment but optimal treatment approaches for vascular risk factors and preventative measures for infections and other systemic complications improve quality of life after stroke.

It is important to determine risk factors associated with stroke patients with poor functional outcomes to identify manageable risk factors. To address this question, we aimed to analyze predictors of increased morbidity of IS patients in a single stroke unit.

Materials and Methods

We included IS patients admitted to the Istanbul University Stroke Unit between July 2014 and September 2020. Diagnosis of stroke was made with computer tomography or magnetic resonance imaging modalities in patients with acute onset neurological symptoms by a stroke neurologist. Patients with cerebral venous thrombosis, intracerebral hemorrhage (subdural, subarachnoid, or intra-parenchymal hemorrhage) and transient ischemic attacks were not included in the study. In addition, patients younger than 18 years old were excluded. The data of all included patients had been recorded in the Istanbul Medical School Stroke Registry (4).

Patients were grouped according to modified Rankin Scale (mRS) score at discharge. Patients with mRS >3 were determined as poor functional outcome group. Even though the conventional tendency is not to include mRS score of 3 as a good outcome, this rule may not be appropriate for evaluation at discharge, but it is more suitable for evaluating third-month functional status. The National Institutes for Health stroke scale (NIHSS) scores were recorded at admission. Gender, diabetes, hypertension, history of previous stroke, ischemic heart disease, hyperlipidemia, diagnosis of pneumonia during hospitalization in the stroke unit and atrial fibrillation were determined as possible indicators for poor functional outcome. To generalize results and implement preventative practices for the daily care of stroke, patients we did not focus on ischemic-stroke subtypes. Istanbul University Faculty of Medicine Local Ethics Committee approved the study protocol (2020/1543).

Statistical Analysis

We used a decision tree method, chi-squared Automatic Interaction Detection (CHAID) to analyze our data set via IBM SPSS (Statistical Package for the Social Sciences) version 25. CHAID is principally a multivariate analysis technique and is used as a prediction model for different fields including neurology (5). CHAID analysis is a very useful tool to analyze big data sets. CHAID is not hypothesis driven and is used to explore associations between different variables. Our stroke data set after applying the inclusion and exclusion criteria consisted of a large amount of patients' records which were suitable for CHAID analysis. Minimum number of cases was set 100 for the parent node and 50 for the child node. Maximum number of levels was 3 for CHAID. The significance level for splitting nodes and merging categories was determined as 0.05. Significance values were adjusted using the Bonferroni method. CHAID method is widely used to analyze stroke databases. Stroke subtype cannot be identified sufficiently with this model but prediction of prognosis and risk factors associated with stroke are satisfactory (6,7,8).

Results

We included 881 patients with IS in the study according to the inclusion and exclusion criteria mentioned above. Demographical and clinical characteristics of patients are shown in Table 1.

CHAID analysis revealed that the most important factor on mRS score >3 was pneumonia (Figure 1). Overall percentage of the model was found at 74% in the classification table for CHAID growing method.

Since pneumonia was found as a significant predictor for poor functional outcome, we analyzed possible risk factors associated with pneumonia. As expected, there was a statistically significant relationship between dysphagia and severe walking disability and pneumonia ($p<0.00$ and $p<0.00$). The mean age was 73.4 (±11.9) years, and the mean NIHSS score was 12.7 (±6.9) in patients who had pneumonia during hospitalization. The mean age and mean

Table 1. Clinical and demographical features of patients

	n=881
Gender, male (n, %)	515, 59%
Age (mean, SD)	66.5±14.4
History of previous stroke* (n, %)	261, 30%
Smoking (n, %)	361, 41%
Hypertension (total, n, %)	642, 73%
Diabetes (total, n, %)	351, 40%
History of transient ischemic attack (n, %)	101, 12%
Coronary artery disease (n, %)	234, 27%
Peripheral arterial disease (n, %)	39, 4%
Hyperlipidemia on admission (n, %)	359, 63%
Hyperlipidemia total, including diagnosis at admission (n, %)	606, 69%
Cancer (n, %)	85, 10%
Atrial fibrillation (n, %)	356, 40%
Pneumonia (n,%)	164, 19%
Recurrent ischemic stroke** (n, %)	38, 4%
NIHSS score (mean, SD)	7.7±6.2
mRS score >3 (n, %)	308, 35%

*History of previous stroke: Ischemic or hemorrhagic ischemic stroke before index stroke.

**Recurrent ischemic stroke: A newly developed ischemic stroke after minimum >48 hours from admission.

1: Patients with modified Rankin Scale scores less than 3 including 3.

2: Patients with modified Rankin Scale scores greater than 3.

n: number, SD: Standard deviation, NIHSS: National Institutes of Health stroke scale, mRS: Modified Rankin Scale score

NISSS score were higher compared to patients without pneumonia. These results were also statistically significant (p<0.00 and p<0.00, respectively).

Smoking was also found as a strong risk factor in those patients who had pneumonia. Finally, smokers with pneumonia accumulated at the atrial fibrillation arm. On the other hand, stroke patients who did not have pneumonia had different risk factors for poor functional outcome. Hypertension and hyperlipidemia composed second and third nodes as a predictor, respectively. Hyperlipidemia should be interpreted with caution depending on the presence of hypertension.

Finally, we analyzed relationship between stroke etiologies and mRS scores (p=0.2). The results are given in Table 2.

Discussion

In this study, we analyzed possible risk factors for poor functional outcome in stroke. We found that pneumonia and hypertension were associated with poor outcome. Stroke patients with pneumonia and smoking history also had increased risk for mRS score >3 at discharge.

Patients with mRS score >3 who did not have pneumonia accumulated in hypertension and hyperlipidemia nodes. Surprisingly, diabetes and gender did not have significant results regarding mRS scores in CHAIDS analysis.

Stroke cases may be complicated with pneumonia, especially aspiration pneumonia (9). Derbisz et al. (10,11) showed that prestroke morbidity and elevated C-reactive protein level are associated with infection in stroke patients who received thrombolysis. Association of infection with functional outcome was also shown in different studies (10,11). We found that patients with pneumonia were older and had greater NIHSS scores. Similar to our results, stroke patients with pneumonia were older, had higher stroke severity, and were more likely to have atrial fibrillation and history of ischemic heart disease compared to stroke patients without infection in a different study (9).

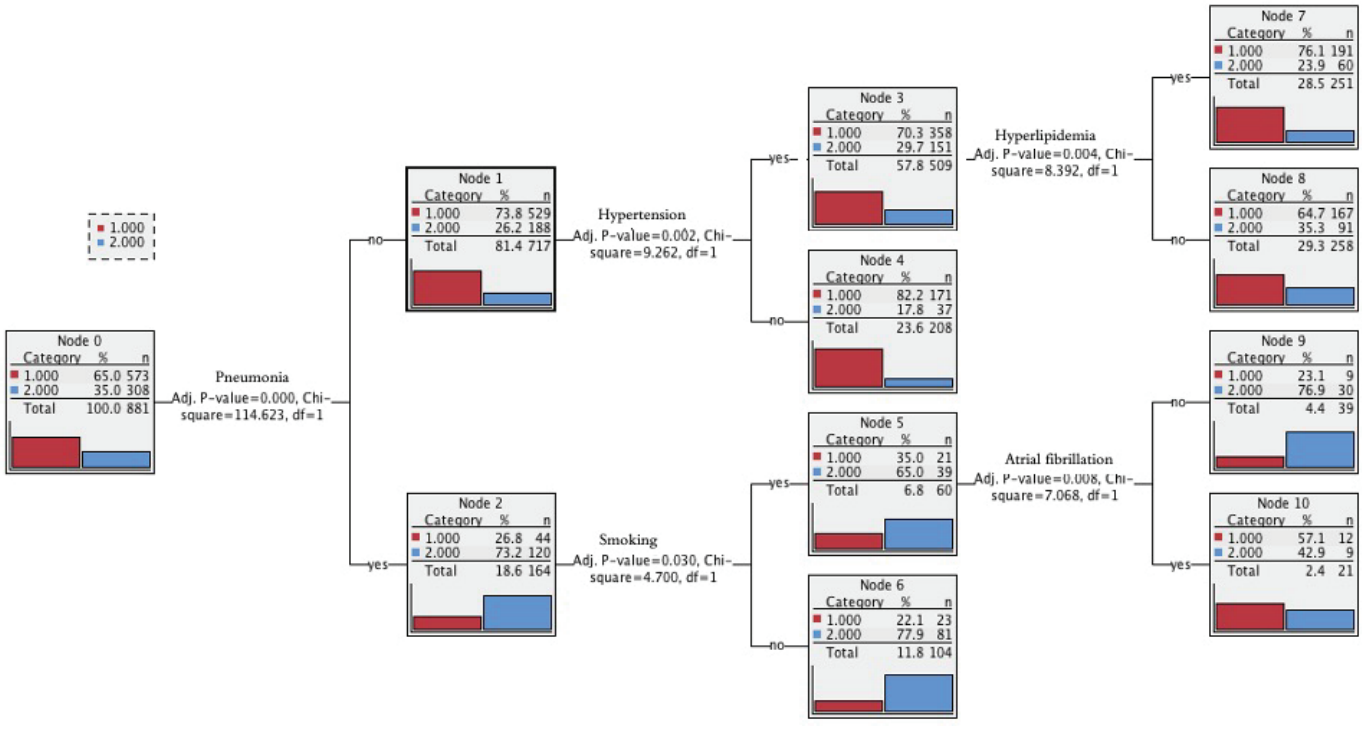

Figure 1. Decision tree results

Table 2. Stroke etiologies and modified Rankin Scale scores

Stroke etiologies	mRS 0	mRS 1	mRS 2	mRS 3	mRS 4	mRS 5	mRS 6
Large artery atherosclerosis (n, %)	20, 11%	33, 18%	29, 16%	38, 21%	41, 22%	18, 10%	0
Cardioembolic stroke (n, %)	37, 12%	61, 20%	44, 15%	52, 17%	66, 21%	43, 14%	1, 0.3%
Small vessel disease (n, %)	4, 13%	7, 22%	6, 19%	6, 19%	5, 16%	3, 19%	0
Undetermined etiology (n, %)	31, 18%	39, 23%	25, 15%	21, 12%	35, 20%	18, 10%	2, 1.2%
>1 etiology (for example; large artery atherosclerosis and cardioembolism)	12, 9%	25, 19%	19, 15%	25, 19%	26, 20%	21, 16%	2, 1.5%
Rare etiologies (dissection, coagulapathies, etc.) (n, %)	14, 28%	8, 16%	3, 6%	6, 12%	14, 28%	5, 10%	0, 0%

mRS: Modified Rankin Scale scores, n: Number, %: Percentage

We did not include stroke severity and NIHSS score to the decision tree analysis intentionally. Primarily, the main purpose of this decision was to understand which elements affected the clinical outcome other than affected brain regions and stroke severity. Another study based on a stroke database from Netherlands supports our findings regarding the association between infection and poor outcome. They also suggest that stroke associated infections are independent risk factors for worse functional outcome in stroke patients (12). Patients who received appropriate treatment (antibacterial, antifungal drugs, etc.) for stroke associated infections were found to have better outcome (13). Hannawi et al. (14) suggested that aspiration and stroke related immunosuppression might explain the pathophysiology of pneumonia in stroke patients.

As our results suggest, it is crucial to avoid in-hospital pneumonia to improve outcome in stroke patients. Many stroke guidelines such as European stroke guidelines do not support the use of prophylactic antibiotic treatments (15). Preventing hospital infections, especially aspiration pneumonia, should be prioritized for every single patient with stroke. Swallow-tests before feeding, treatment of fever and urinary care are well-known preventative measures. Nevertheless, these simple measures can be ignored very easily and may lead to undesirable consequences.

Study Limitations

There are some limitations of this study. Firstly, even though our stroke database was registered by a neurologist and reviewed by experienced stroke neurologists, it is based on a single center experience. Secondly, this study is a retrospective observational study and therefore selection bias could not be entirely excluded.

Conclusion

In conclusion, to achieve better outcomes in patients with stroke, preventative measures should not be limited to only secondary prophylaxis. Avoiding infections plays an essential role. New data-driven approaches might be beneficial in stroke registry data research.

Ethics

Ethics Committee Approval: Istanbul University Faculty of Medicine Local Ethics Committee approved the study protocol (2020/1543).

Informed Consent: Obtained from patients and/or their relatives.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.S., M.G.G., N.Y., Design: M.S., M.G.G., Data Collection or Processing: M.S., N.Y., Analysis or Interpretation: M.S., M.G.G., Literature Search: M.S., Writing: M.S., N.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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