

## Evaluation of the Association of Serum Uric Acid Levels and Stroke in Emergency Department Patients

Acil Servis Hastalarında Serum Ürik Asit Düzeyi ve İnme İlişkisinin Değerlendirilmesi

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### ABSTRACT

**Aim:** Stroke is a leading cause of disability and fatality. While clinical and imaging methods are commonly used in stroke management, biochemical parameters such as serum uric acid (SUA) level are largely overlooked. This study aimed to examine the relationship between high or low SUA levels and both ischemic and hemorrhagic stroke.

**Material and Methods:** This is a retrospective, single-center observational study. The study included all consecutive patients who were consulted from the emergency department (ED) to neurology and/or neurosurgery between January 1, 2023, and December 31, 2023. Data of the patients were obtained from the hospital computer system and ED records. While SUA levels of  $\leq 2.8$  mg/dL indicated hypouricemia, levels of  $\geq 7$  mg/dL were considered hyperuricemia.

**Results:** A total of 1186 adult patients were included in the study. It was observed that 484 of them were diagnosed with stroke, 394 were ischemic stroke, and 90 were hemorrhagic stroke. Stroke patients had higher median SUA levels ( $p < 0.001$ ). The median SUA level of ischemic stroke patients was higher than hemorrhagic stroke patients ( $p < 0.001$ ). Hyperuricemia increased the risk of ischemic stroke 2.4-fold (OR: 2.402, 95% CI: 1.792-3.221,  $p < 0.001$ ). Hypouricemia decreased the risk of ischemic stroke (OR: 0.272, 95% CI: 0.129-0.577,  $p < 0.001$ ).

**Conclusion:** SUA levels are associated with stroke and ischemic stroke. Hyperuricemia may be useful as an additional parameter to strengthen the diagnosis of possible stroke in ED. SUA levels of patients at risk for stroke can be useful in terms of follow-up of these patients and the precautions to be planned.

**Keywords:** Emergency department; stroke; uric acid.

### ÖZ

**Amaç:** İnme, sakatlık ve ölümlerin önde gelen nedenlerinden biridir. İnme yönetiminde klinik ve görüntüleme yöntemleri yaygın olarak kullanılırken, serum ürik asit (SUA) düzeyi gibi biyokimyasal parametreler büyük ölçüde göz ardı edilmektedir. Bu çalışmada, yüksek veya düşük SUA düzeyleri ile hem iskemik hem de hemorajik inme arasındaki ilişkinin incelenmesi amaçlanmıştır.

**Gereç ve Yöntemler:** Bu çalışma retrospektif, tek merkezli gözlemsel bir çalışmadır. Çalışmaya 1 Ocak 2023 ile 31 Aralık 2023 tarihleri arasında acil servisten nöroloji ve/veya beyin cerrahisine konsülte edilen tüm ardışık hastalar dahil edilmiştir. Hastaların verileri hastane bilgisayar sisteminden ve acil servis kayıtlarından elde edilmiştir.  $\leq 2,8$  mg/dL olan SUA düzeyleri hipourisemiye gösterirken,  $\geq 7$  mg/dL olması hiperurisemi olarak kabul edildi.

**Bulgular:** Çalışmaya toplam 1186 yetişkin hasta dahil edildi. Bunların 484'ünün inme tanısı aldığı, 394'ünün iskemik inme, 90'ının ise hemorajik inme olduğu görüldü. İnme hastalarının medyan SUA düzeyleri daha yüksekti ( $p < 0,001$ ). İskemik inme hastalarının medyan SUA düzeyi hemorajik inme hastalarından daha yüksekti ( $p < 0,001$ ). Hiperurisemi iskemik inme riskini 2,4 kat artırmıştır (OR: 2,402; %95 GA: 1,792-3,221;  $p < 0,001$ ). Hipourisemi iskemik inme riskini azaltmıştır (OR: 0,272; %95 GA: 0,129-0,577;  $p < 0,001$ ).

**Sonuç:** SUA düzeyleri inme ve iskemik inme ile ilişkilidir. Hiperurisemi, acil serviste olası inme tanısını güçlendiren ek bir parametre olarak yararlı olabilir. İnme açısından riskli hastaların SUA düzeyleri bu hastaların takibi ve planlanacak önlemler açısından faydalı olabilir.

**Anahtar kelimeler:** Acil servis; inme; ürik asit.

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## INTRODUCTION

Stroke is one of the leading causes of mortality and disability worldwide and stroke is thought to be responsible for 11% of deaths (1). According to estimates, there were 9.5 million new stroke cases and 2.7 million deaths in 2016. 50% of people who become disabled due to stroke complications are under the age of 70, which increases the burden of stroke on the healthcare system and expenditures. The vast majority of strokes are ischemic strokes. Although less common, hemorrhagic strokes are also a cause of serious mortality and morbidity (2,3). Hypertension, diabetes mellitus, obesity, and cardiovascular diseases are known risk factors for stroke (4-7). In addition, studies have shown that high serum uric acid (SUA) level, i.e. hyperuricemia, increases the risk of stroke (2,5,8-10). Uric acid is produced in the human body as a result of the metabolism of purine nucleotides. The majority of uric acid is excreted through the kidneys and the rest through the intestines. Uric acid is an important antioxidant and is involved in the scavenging of free radicals. Hypouricemia causes a decrease in antioxidant capacity and all tissues and organs are exposed to oxidative stress (11,12). SUA levels show differences between societies and genders. Normal SUA levels are generally shown between 3 mg/dl and 6.8 mg/dl in the literature (11,13).

It is known that SUA level has a u-shaped effect on renal diseases, cardiovascular diseases, and all-cause mortality, both low and high levels increase the risk (13-15). Studies suggesting that hypouricemia is associated with neurological diseases such as Parkinson's, Alzheimer's, and multiple sclerosis are also available in the literature (16-18).

Studies in the literature examining the association between stroke and SUA levels generally focus on the association between hyperuricemia and ischemic stroke. Although the strong association between hyperuricemia and ischemic stroke has been demonstrated in many studies in the literature, studies showing the effect of hypouricemia on the development of ischemic stroke have remained limited. On the other hand, studies examining the effect of SUA levels on the development of hemorrhagic stroke are also very limited. This study aimed to investigate the effects of low and high SUA levels on the development of ischemic and hemorrhagic stroke.

## MATERIAL AND METHODS

### Study Setting and Design

This is a retrospective, single-center observational study. It was performed in the emergency department (ED) of a tertiary university hospital in Turkey with approximately 120,000 admissions per year. The study was initiated after local ethics committee approval (Non-Invasive Health Research Ethics Committee of Düzce University, approval ID: 2024/13, dated: February 5, 2024) was obtained. The study was conducted on patients aged 18 years and older who were admitted to the ED between January 1, 2023, and, December 31, 2023.

Adult patients admitted to the ED during the indicated period who were consulted with neurology or neurosurgery departments were identified through the hospital computer system and included in the study. Data on admission diagnosis, comorbid disease, computed tomography (CT) and diffusion magnetic resonance imaging (MRI) reports, consultation reports, SUA, and

serum electrolyte levels were obtained from the hospital computer system and ED archive records.

### Selection of Participants and Study Protocol

All patients admitted to the ED department aged 18 years and old, being consulted to neurology and/or neurosurgery departments from the ED were included in the study. Patients with incomplete data, patients without CT or MRI examination, pregnant women, and patients referred to our hospital from another hospital were excluded from the study. Among the total of 116,916 ED admissions during the study period, the number of admissions aged 18 years and over was 110,469.

Normal values of SUA level have been shown to range between 3 mg/dl and 6.8 mg/dl in various studies (11,13). There are also studies in which the normal range of uric acid was determined differently according to gender (2,5). In this study, patients with SUA level  $\leq 2.8$  mg/dl for both gender groups were grouped as hypouricemic patients. Patients with SUA level  $\geq 7$  mg/dl were grouped as hyperuricemic patients, again valid for both gender groups. The other values were named normouricemia.

The diagnoses of stroke, hemorrhagic stroke, and ischemic stroke were obtained from the consultation notes written by neurologists and/or neurosurgeons after evaluation of the patient's clinical condition and CT and/or MRI imaging findings. Descriptive statistical data of the patients included in the study in terms of the scanned parameters were generated. Stroke and non-stroke patient groups were compared with each other in terms of the characteristics screened in the study. Ischemic stroke and hemorrhagic stroke groups were compared in terms of demographic data, SUA levels, and serum electrolyte levels. Odds ratio values were calculated for the development of ischemic and hemorrhagic stroke in hyperuricemia, hypouricemia, and comorbid diseases screened in the study. Finally, patients were divided into 3 groups, hypouricemic, normouricemic, and hyperuricemic according to SUA values, and comparisons were made between the groups in terms of the parameters screened in the study.

### Statistical Analysis

Compliance with normal distribution was evaluated by the Kolmogorov-Smirnov test, Shapiro-Wilk test, and histogram. Continuous data were compared between two groups by the Mann-Whitney U test and between three groups by the Kruskal-Wallis test. The relationship between categorical variables was analyzed by Pearson's chi-square test or Fisher's exact test. Bonferroni correction was applied since three group comparisons were made. Continuous data were summarized by median, 25<sup>th</sup> and 75<sup>th</sup> percentile, minimum-maximum, and categorical data were summarized by frequency and percentage. Statistical software IBM SPSS v.23 was used for these analyses. The significance level was set as  $p < 0.05$ .

## RESULTS

During the study period, 1186 patients were consulted from the ED to the neurology and/or neurosurgery department. 64 patients had an SUA level of  $\leq 2.8$  while 231 patients had an SUA level of 7 mg/dl or higher. Out of all the patients included in the study, 484 were diagnosed with stroke in the ED. Among these patients, 394 were diagnosed with ischemic stroke and 90 were diagnosed

with hemorrhagic stroke. The median age of the patients included in the study was 68 (range, 18-97) years and 48.2% (n=572) of the patients were female. The median age of the patients with a diagnosis other than stroke was 65 (range, 18-97), and the median age of patients with a diagnosis of stroke was 72 (range, 21-97) years. The median age of stroke patients was statistically significantly higher ( $p<0.001$ ). There was no significant difference in gender between stroke and non-stroke patients ( $p=0.866$ ). The median SUA level of all the patients included in the study was 5.3 mg/dL, while this level was 5.1 mg/dL in non-stroke patients and 5.7 mg/dL in stroke patients. The median SUA level was statistically significantly higher in stroke patients ( $p<0.001$ ). The most common comorbid diseases included in the study were hypertension at 56.9% (n=675), diabetes mellitus at 32.5% (n=386), and cardiac diseases at 33.1% (n=393). The hypertension rate

was 47.6% (n=334) in non-stroke patients and 70.5% (n=341) in stroke patients and there was a significant difference between the groups ( $p<0.001$ ). Comorbid diseases and median electrolyte levels, and comparisons between stroke and non-stroke patient groups were shown in Table 1.

The median age of ischemic stroke patients in the study was 71.5 (range, 21-97) years and 48.7% (n=192) were female. In hemorrhagic stroke patients, the median age was 73 (range, 38-96) years and the female sex ratio was 44.4% (n=40). There was no significant difference between hemorrhagic and ischemic stroke groups in terms of age ( $p=0.803$ ) and gender ( $p=0.463$ ). The median SUA level of ischemic stroke patients was significantly higher than hemorrhagic stroke patients (5.8 vs 5.1 mg/dL,  $p<0.001$ ). Comparison of ischemic stroke and hemorrhagic stroke patients in terms of age, gender, SUA, and serum electrolyte levels were shown in Table 2.

**Table 1.** Comparison of characteristic features and serum electrolyte levels among patients with and without stroke

	Non-Stroke (n=702)	Stroke (n=484)	p
Age (years)*	65 (48-77) [18-97]	72 (63-80) [21-97]	<0.001
Gender (female), n (%)	340 (48.4)	232 (47.9)	0.866
Uric Acid (mg/dL)	5.1 (4.0-6.2) [1.0-16.1]	5.7 (4.6-7.0) [2.1-20.6]	<0.001
Sodium (Meq/L)	138 (136-140) [112-172]	138 (136-140) [123-168]	0.230
Potassium (Meq/L)	4.20 (3.91-4.58) [2.37-6.95]	4.36 (4.00-4.72) [2.92-5.97]	<0.001
Chloride (Meq/L)	103 (99-105) [76-130]	103 (101-105) [81-121]	0.038
Calcium (mg/dL)	9.2 (8.9-9.6) [5.5-13.7]	9.3 (8.9-9.6) [6.7-16.9]	0.140
Phosphate (mg/dL)	3.21 (2.69-3.72) [0.76-9.14]	3.27 (2.84-3.75) [0.87-8.78]	0.126
Magnesium (mg/dL)	1.98 (1.82-2.11) [0.99-3.37]	1.97 (1.82-2.11) [1.10-3.19]	0.959
Hypertension, n (%)	334 (47.6)	341 (70.5)	<0.001
Diabetes Mellitus, n (%)	204 (29.1)	182 (37.6)	0.002
Heart Diseases, n (%)	206 (29.3)	187 (38.6)	<0.001
Asthma and COPD, n (%)	61 (8.7)	46 (9.5)	0.630
Renal Failure, n (%)	26 (3.7)	15 (3.1)	0.570
Malignancies, n (%)	78 (11.1)	36 (7.4)	0.035
History of Stroke, n (%)	104 (14.8)	93 (19.2)	0.045

COPD: chronic obstructive pulmonary disease, \*: values presented as median (interquartile range, 25<sup>th</sup>-75<sup>th</sup> percentile) [minimum-maximum]

**Table 2.** Comparison of characteristic features and serum electrolyte levels among patients with ischemic and hemorrhagic stroke

	Ischemic Stroke (n=394)	Hemorrhagic Stroke (n=90)	p
Age (years)*	71.5 (64-80) [21-97]	73 (59-80) [38-96]	0.803
Gender (female), n (%)	192 (48.7)	40 (44.4)	0.463
Uric Acid (mg/dL)	5.8 (4.8-7.2) [2.3-20.6]	5.1 (4.1-6.3) [2.1-12.5]	<0.001
Sodium (Meq/L)	138 (136-140) [123-168]	139 (137-141) [126-150]	0.013
Potassium (Meq/L)	4.40 (4.00-4.79) [2.92-5.91]	4.11 (3.73-4.56) [3.10-5.97]	<0.001
Chloride (Meq/L)	103 (100-105) [82-121]	104 (102-106) [81-113]	0.098
Calcium (mg/dL)	9.3 (8.9-9.6) [6.7-11.9]	9.3 (9.0-9.5) [8.1-10.9]	0.488
Phosphate (mg/dL)	3.28 (2.86-3.75) [0.90-8.28]	3.25 (2.77-3.80) [0.87-6.29]	0.707
Magnesium (mg/dL)	1.97 (1.82-2.11) [1.10-3.19]	1.97 (1.85-2.10) [1.37-3.03]	0.611
Hypertension, n (%)	281 (71.3)	60 (66.7)	0.383
Diabetes Mellitus, n (%)	157 (39.8)	25 (27.8)	0.033
Heart Diseases, n (%)	162 (41.1)	25 (27.8)	0.019
Asthma and COPD, n (%)	39 (9.9)	7 (7.8)	0.536
Renal Failure, n (%)	12 (3.0)	3 (3.3)	0.887
Malignancies, n (%)	32 (8.1)	4 (4.4)	0.230
History of Stroke, n (%)	75 (19.0)	18 (20.0)	0.834

COPD: chronic obstructive pulmonary disease, \*: values presented as median (interquartile range, 25<sup>th</sup>-75<sup>th</sup> percentile) [minimum-maximum]

The presence of hyperuricemia increased the risk of ischemic stroke 2.4-fold (OR: 2.402, 95% CI: 1.792-3.221,  $p < 0.001$ ). In the presence of hypouricemia, the risk of ischemic stroke was significantly reduced (OR: 0.272, 95% CI: 0.129-0.577,  $p < 0.001$ ). In the presence of hypertension, the risk of ischemic stroke increased 2.5-fold (OR: 2.512, 95% CI: 1.939-3.255,  $p < 0.001$ ). Diabetes mellitus increased the risk of ischemic stroke 1.6-fold (OR: 1.629, 95% CI: 1.264-2.099,  $p < 0.001$ ) and heart disease increased the risk of ischemic stroke approximately 1.7-fold (OR: 1.696, 95% CI: 1.317-2.183,  $p < 0.001$ ). When similar comparisons were made between the hemorrhagic stroke group and the non-hemorrhagic stroke group, no significant results were obtained showing that hyperuricemia, hypouricemia, hypertension, diabetes mellitus, heart diseases, or history of stroke caused an increase or decrease in the risk of hemorrhagic stroke. The effects of hyperuricemia, hypouricemia, and comorbid diseases on the risk of ischemic and hemorrhagic stroke were shown in Table 3. The rate of hypertension was 46.9% (n=30) in the hypouricemic group, 54.0% (n=481) in the normouricemic group, and 71.0% (n=164) in the hyperuricemic group. There was a significant difference in the rate of hypertension between SUA groups and the rate of hypertension was higher in the hyperuricemic group ( $p < 0.001$ ). The stroke rate was 21.9% (n=14) in the hypouricemia group, and 38.4% (n=342), and 55.4% (n=128) in the normouricemia and hyperuricemia groups, respectively. Stroke rates were significantly different in all three SUA groups and stroke rate was higher in the hyperuricemia group ( $p < 0.001$ ). When SUA groups were compared in terms of ischemic

stroke, the rates of all three groups were significantly different and the rate of ischemic stroke was higher in the hyperuricemia group (12.5%, n=8 vs 30.4%, n=271, vs 49.8%, n=115,  $p < 0.001$ ). No significant difference was found between SUA groups in terms of hemorrhagic stroke rates (9.4%, n=6, vs 8.0%, n=71, vs 5.6%, n=13,  $p = 0.419$ ). Comparisons between SUA-level groups in terms of age, gender, comorbid diseases, and stroke types were shown in Table 4.

**DISCUSSION**

Stroke is one of the most important causes of mortality and disability in today's world. Stroke at an early age can lead to early death as well as long life expectancy with disability. The ages at which stroke occurs differ between societies and geographies. In studies performed in Eastern societies where the population is relatively poorer, stroke is usually seen frequently in the 60s, whereas in Western societies, which are more socioeconomically developed, stroke cases become more frequent after the 70s. In some studies performed in different societies, stroke rates were found to be higher in male patients and some female patients (6,8,19-21). In our study, the median age of stroke patients was 72 years and this result is similar to Western societies with better economic conditions. In Turkey, the country where the study was conducted, this situation should be attributed to easy access to health services and effective treatments for diseases that increase the risk of stroke due to the social state policies implemented rather than to better economic conditions. In our study, no significant difference was found between genders in terms of stroke rates.

**Table 3.** Comparison of the patients with ischemic stroke to those without, and patients with hemorrhagic stroke to those without, based on the serum uric acid levels and comorbidities

	Ischemic Stroke (n=394)			Hemorrhagic Stroke (n=90)		
	OR	95% CI	p	OR	95% CI	p
<b>Hypouricemia</b> (SUA $\leq 2.8$ mg/dL)	0.272	0.129-0.577	<b>&lt;0.001</b>	1.278	0.536-3.050	0.579
<b>Hyperuricemia</b> (SUA $\geq 7$ mg/dL)	2.402	1.792-3.221	<b>&lt;0.001</b>	0.680	0.371-1.247	0.210
<b>Hypertension</b>	2.512	1.939-3.255	<b>&lt;0.001</b>	1.564	0.993-2.464	0.054
<b>Diabetes Mellitus</b>	1.629	1.264-2.099	<b>&lt;0.001</b>	0.783	0.485-1.263	0.315
<b>Heart Diseases</b>	1.696	1.317-2.183	<b>&lt;0.001</b>	0.761	0.472-1.227	0.261
<b>History of Stroke</b>	1.291	0.940-1.773	0.113	1.281	0.746-2.199	0.369

SUA: serum uric acid, OR: odds ratio, CI: confidence interval

**Table 4.** Comparison of SUA-level groups in terms of demographic data, comorbid diseases, and stroke diagnoses

	Hypouricemia	Normouricemia	Hyperuricemia	P <sup>#</sup>
	SUA $\leq 2.8$ mg/dL (n=64)	SUA 2.9-6.9 mg/dL (n=891)	SUA $\geq 7$ mg/dL (n=231)	
<b>Age (years)*</b>	62 (45-74) [20-90] <sup>a</sup>	68 (53-78) [18-97] <sup>a</sup>	74 (64-82) [21-97] <sup>b</sup>	<b>&lt;0.001</b>
<b>Gender (female), n (%)</b>	51 (79.7) <sup>a</sup>	409 (45.9) <sup>b</sup>	112 (48.5) <sup>b</sup>	<b>&lt;0.001</b>
<b>Hypertension, n (%)</b>	30 (46.9) <sup>a</sup>	481 (54.0) <sup>a</sup>	164 (71.0) <sup>b</sup>	<b>&lt;0.001</b>
<b>Diabetes Mellitus, n (%)</b>	21 (32.8) <sup>a,b</sup>	274 (30.8) <sup>b</sup>	91 (39.4) <sup>a</sup>	0.044
<b>Heart Diseases, n (%)</b>	13 (20.3) <sup>a</sup>	275 (30.9) <sup>a</sup>	105 (45.5) <sup>b</sup>	<b>&lt;0.001</b>
<b>History of Stroke, n (%)</b>	10 (15.6) <sup>a,b</sup>	137 (15.4) <sup>b</sup>	50 (21.6) <sup>a</sup>	0.072
<b>Malignancies, n (%)</b>	9 (14.1) <sup>a</sup>	79 (8.9) <sup>a</sup>	26 (11.3) <sup>a</sup>	0.253
<b>Stroke, n (%)</b>	14 (21.9) <sup>a</sup>	342 (38.4) <sup>b</sup>	128 (55.4) <sup>c</sup>	<b>&lt;0.001</b>
<b>Ischemic Stroke, n (%)</b>	8 (12.5) <sup>a</sup>	271(30.4) <sup>b</sup>	115 (49.8) <sup>c</sup>	<b>&lt;0.001</b>
<b>Hemorrhagic Stroke, n (%)</b>	6 (9.4) <sup>a</sup>	71 (8.0) <sup>a</sup>	13 (5.6) <sup>a</sup>	0.419

SUA: serum uric acid, #: Bonferroni correction was applied since three group comparisons were made ( $p < 0.016$  indicates a statistically significant difference, <sup>a,b,c</sup>: different letters written as exponents indicate statistically significant differences, \*: values presented as median (interquartile range, 25<sup>th</sup>-75<sup>th</sup> percentile) [minimum-maximum]

In the literature, the rate of ischemic strokes in all strokes is shown to be between 70% and 87% (2,4,19,20,22). In our present study, ischemic strokes constitute more than 80% of all stroke patients and our findings are similar to the literature.

Hypertension, diabetes mellitus, cardiovascular diseases, and dyslipidemias are comorbid diseases which are risk factors for stroke (5,6,8,19,21). Studies have shown that more than 60% of stroke patients have high arterial blood pressure values measured at presentation and more than 70% of stroke patients, whether hemorrhagic or ischemic, have a diagnosis of hypertension (23). In our study, the most common comorbid diseases in stroke patients were hypertension, cardiovascular diseases, and diabetes mellitus. All three of these comorbid diseases are observed at a higher rate in stroke patients than in non-stroke patients. The diagnosis of hypertension reaches 70% in the stroke patient group. This is similar to the literature and clearly demonstrates the relationship between hypertension and stroke. In our study, hypertension increased the risk of ischemic stroke approximately 2.5 times. In terms of hemorrhagic stroke, no statistically significant increase in risk due to hypertension was found, contrary to the findings in the literature. It is thought that further studies with a larger sample size and a more general population will provide results on the relationship between hemorrhagic stroke and hypertension that will match the data in the literature. In our study, the risk of ischemic stroke increased approximately 1.6-fold in the presence of cardiovascular disease and 1.6-fold in the presence of diabetes mellitus. No significant increase in the risk of hemorrhagic stroke due to comorbid diseases was detected.

There are many studies showing that hyperuricemia is a risk factor for ischemic stroke (2,5,8-10). It is also known that comorbid diseases including hypertension, diabetes mellitus, and cardiovascular diseases which increase the risk of stroke are observed more frequently in hyperuricemic patients (2,11,12,24). In our study, median uric acid level was significantly higher in stroke patients compared with non-stroke patients. In our study, the rate of ischemic stroke was also significantly higher in the hyperuricemic patient group and hyperuricemia increased the risk of ischemic stroke approximately 2.4-fold. Our findings in terms of the relationship between hyperuricemia and ischemic stroke are similar to the literature. The first diagnosis of many diseases is made in EDs. The diagnostic power of EDs depends on the clinical experience of the physicians working there as well as the available tests and imaging methods. In many health centers other than tertiary care, MRI or CT examination to confirm the diagnosis of stroke cannot be performed. In the light of the findings of our study, it can be said that hyperuricemia is an additional parameter to strengthen the preliminary diagnosis of stroke in patients presenting to EDs with symptoms suspicious for stroke. Hyperuricemic patients presenting with stroke-like symptoms to an ED where CT or MRI imaging cannot be performed may be given priority over normouricemic patients when referring to centers where imaging can be performed.

There are no adequate studies in the literature on the relationship between hypouricemia and stroke. The findings of our study show that both stroke and ischemic

stroke rates were significantly lower in the hypouricemic patient group. In addition, the risk of ischemic stroke was significantly lower in hypouricemic patients compared to non-hypouricemic patients. Hypouricemia detected in patients admitted to the ED with findings suspicious for stroke may give ED physicians an idea that the patient may not have an ischemic stroke. However, the final diagnosis should be made by imaging modalities such as CT and MRI.

Adding SUA levels to the blood parameters checked during hospital admissions or health screenings of patients at risk for stroke will be beneficial for the follow-up of these patients. In patients with hyperuricemia, performing the necessary tests for hypertension, diabetes mellitus, and cardiovascular diseases, which are known to increase the risk of stroke, and starting treatment immediately if these diseases are detected may be beneficial in minimizing the risk of stroke.

There are few studies showing that SUA-lowering treatments are associated with a lower stroke risk (25). In the light of our findings, we think that SUA-lowering treatments may reduce the risk of ischemic stroke in normouricemic and hyperuricemic patients who are at risk for ischemic stroke. Further studies on this subject will contribute to the literature.

In our study, no difference was found between the groups formed according to SUA levels in terms of hemorrhagic stroke rates, and no significant conclusion was reached regarding whether hyperuricemia or hypouricemia increases or decreases the risk of hemorrhagic stroke. In our search, we found that one study concluded that high SUA levels increased the risk of hemorrhagic stroke (4). However, we could not find any data on the relationship between hemorrhagic stroke and SUA levels except for the mentioned study. Our study shows that SUA levels are not related to the development of hemorrhagic stroke and in this respect, it is not similar to the other study, further studies will provide a better understanding of the subject. Firstly, our study is single-center and retrospective. Secondly, SUA level was measured once in each patient in the study; SUA levels before or after admission are not known. Thirdly, urinary uric acid was not measured in the study; the causes of hypouricemia or hyperuricemia cannot be known. Fourthly, the medications used by the patients were not evaluated in our study; it is not known whether the patients were taking medications that may affect SUA levels.

## CONCLUSION

Hypertension is the comorbid disease that increases the risk of ischemic stroke the most (approximately 2.5-fold) and 70% of stroke patients have hypertension. Stroke and ischemic stroke patients have higher median uric acid levels and hyperuricemia rates. Hyperuricemia increases the risk of ischemic stroke approximately 2.4 times. Hypouricemia decreases the risk of ischemic stroke. There is no such relationship in terms of hemorrhagic stroke. In patients who present to the ED with findings suspicious for stroke but in whom MRI or CT cannot be performed, SUA level may give the physician an idea about the preliminary diagnosis. SUA level to be examined during the follow-up of patients at risk for ischemic stroke may be useful in terms of stroke risk assessment.

**Ethics Committee Approval:** The study was approved by the Non-Invasive Health Research Ethics Committee of Düzce University (05.02.2024, 2024/13).

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