JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.969181
J Contemp Med 2022;12(1):86-90

Original Article / Orijinal Araştırma

The Risk Factors for Delirium in Patients with Stroke in Palliative Care

Palyatif Bakımda İnmeli Hastalarda Deliryum İçin Risk Faktörleri

Gülhan Sarıçam[1], Orkun Sarıçam[2]

[1]Pursaklar State Hospital, Department of Neurology Clinic, Ankara, Turkey
[2]Pursaklar State Hospital, Department of Internal Medicine Clinic, Ankara, Turkey

Abstract

Aim: Post-stroke delirium is an acute neuropsychiatric syndrome that increases the distress of patients and family members and leads to long-term results, especially in older age. In this study, we aimed to investigate the risk factors for delirium in patients followed-up in palliative care with the diagnosis of stroke.

Material and Method: This retrospective study included 161 patients followed-up in the palliative care ward with the diagnosis of stroke. Patients diagnosed with stroke were grouped as ischemic stroke (IS), hemorrhagic stroke (HS) and subarachnoid hemorrhage (SAH). The age, gender, Glasgow coma scale (GCS), percutaneous endoscopic gastrostomy (PEG) status, presence of infection, electrolyte values, length of hospitalization, discharge conditions and comorbid diseases of the patients included in the study were evaluated.

Results: The average age of the patients was 70.49±15.269 years, the length of hospitalization was 46.6±16.11 days, and 35 (21.1%) patients had been diagnosed with delirium. In patients who developed delirium, the ages were significantly lower, the infection rates were significantly higher, and the length of hospitalization was significantly longer (p=0.046, p<0.001, p=0.003). While the proportion of patients with a PEG was significantly lower, the rate use of anticholinergics, narcotic analgesics, antiepileptics and antipsychotics was significantly higher in patients who had developed delirium.

Conclusion: We think that determining and managing the risk factors for delirium development in stroke patients followed-up in palliative care will decrease the morbidity and improve the quality of life of the patients and that further studies on this topic are needed.

Keyword: Palliative care, stroke, delirium, length of hospitalization

Öz

Amaç: İnme sonrası deliryum, hastaların ve aile üyelerinin sıkıntısını arttıran ve özellikle ileri yaşlarda uzun süreli sonuçlara yol açan akut nöropsikiyatrik bir sendromdur. Biz bu çalışmada palyatif bakımda stroke tanısı ile izlenen hastalarda deliryum için risk faktörlerini araştırmayı amaçladık.

Gereç ve Yöntem: Bu retrospektif çalışmaya palyatif bakım servisinde stroke tanısı ile izlenen 161 hasta dahil edildi. İnme tanılı hastalar iskemik inme (IS), hemorajik inme (HS) ve subaraknoid kanama (SAK) olarak gruplandırıldı. Çalışmaya alınan hastaların yaşları, cinsiyetleri, glaskow koma skalaları (GKS), perkütan endoskopik gastrostomi (PEG), enfeksiyon varlığı, elektrolit değerleri, ilaç kullanımı, yatış süreleri, çıkış durumları ve komorbid hastalıkları değerlendirildi.

Bulgular: Hastaların yaş ortalamaları 70,49±15,269 yıl, yatış süreleri 46.6±16.11 gündü ve 35 (%21.1) hasta deliryum tanısı aldı. Deliryum gelişen hastaların yaşları anlamlı derecede daha düşük, enfeksiyon oranları anlamlı derecede fazla ve yatış süreleri anlamlı derecede uzundu (p=0.046, p<0.001, p=0.003). Deliryum gelişen hastalarda PEG olanların oranı anlamlı derecede azken, antikolinerjik, narkotik analjezik, antiepileptik ve antipiskotik kullananların oranı anlamlı derecede daha fazlaydı.

Sonuçlar: Palyatif bakımda izlenen inmeli hastalarda deliryum gelişimindeki risk faktörlerinin belirlenip iyi yönetilmesinin, hastaların morbiditelerini azaltıp, yaşam kalitelerini iyileştireceğini ve bu konuda daha fazla çalışmaya ihtiyaç olduğunu düşünüyoruz.

Anahtar Kelime: Palyatif bakım, stroke, deliryum, hastanede yatış süresi

Corresponding *(İletişim)*: Gülhan Sarıçam, Department of Neurology Clinic, Ankara Pursaklar State Hospital, Mimar Sinan Mah. Çağatay Sok. No:39 Ankara, Turkey
E-mail *(E-posta)*: gulhansar01@hotmail.com
Received *(Geliş Tarihi)*: 09.07.2021 **Accepted *(Kabul Tarihi)*:** 04.11.2021

INTRODUCTION

Delirium is defined as a disorder of awareness and cognition (mostly attention and memory); it develops within hours or days, cannot be explained by other cognitive disorders such as dementia, and is a direct result of a physical condition or medication.[1] Unlike many serious diseases, stroke is a sudden and unexpected condition, and it is a leading cause of severe long-term disability.[2] Post-stroke delirium is an acute neuropsychiatric syndrome that increases the distress of patients and family members and leads to long-term results, especially in older age.[3,4]

The palliative care needs of patients after stroke are extensive and evident.[5] Patients are directed to palliative care after stroke for end-of-life decisions rather than symptom management.[6,7] Stroke patients seen by palliative care specialists are more functionally impaired, less likely to possess decision-making capacity and more likely to die in the hospital.[6] Stroke itself is a known predisposing factor for delirium.[3] Studies have reported that the frequency of delirium varies between 12% and 43% in patients with ischemic stroke (IS) and hemorrhagic stroke (HS).[8,9] It has been reported that the prevalence of delirium is 13-42% in patients receiving inpatient palliative care, and that it increases to 88% at the end of life (weeks to hours before death). However, we found no literature on the delirium rates of stroke patients in palliative care.[10]

The pathophysiology of delirium is multifactorial and not fully understood. There are some risk factors for delirium such as advanced age, male gender, an underlying cognitive disorder, medication use, electrolyte disorders, infection, fever, orthopedic and cardiovascular surgeries.[11] In this study, we aimed to investigate the risk factors for delirium in patients diagnosed with stroke followed-up in palliative care.

MATERIAL AND METHOD

The retrospective study was approved by Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital Ethics Committee (Date: 08.07.2020, Decision No:2020-07/682). All procedures were applied per the principles of the Declaration of Helsinki. The files of 161 patients who had been followed-up with the diagnosis of stroke in the palliative care center (PCC) of our hospital between 2015-2020 were reviewed retrospectively. Patients diagnosed with stroke were classified as ischemic stroke (IS), hemorrhagic stroke (HS) and subarachnoid hemorrhage (SAH). The age, gender, Glasgow coma scale (GCS), percutaneous endoscopic gastrostomy (PEG) status, presence of infection, electrolyte values, length of hospitalization, discharge conditions, and comorbid diseases of the patients included in the study were evaluated. Comorbid diseases were classified as dementia, heart disease (HD), hypertension (HT) and diabetes mellitus (DM).

The study collected the data from the medical records written by psychiatrists who had evaluated the patients. The delirium diagnosis was determined using the "Confusion Assessment Method" (CAM) survey.[12] The presence of infection was defined by laboratory tests, identification of pathogens in a bacterial culture or empirical use of antibiotics. The kidney function was evaluated by calculating the blood urea nitrogen (BUN) and plasma creatinine levels and the liver functions by blood aspartate transaminase (AST) and alanine transaminase (ALT) levels, as well as plasma albumin levels. Electrolyte imbalance was assessed by determining the levels of sodium and potassium. The medications used by patients were classified as antipsychotics, anticholinergics, antiepileptics and narcotic analgesics.

Statistical Analyses

The study data comprised 161 individuals. The analyses were performed using the IBM SPSS statistics 23 software bundle. While evaluating the study data, number were given for the categorical variables and descriptive statistics (mean, standard deviation, median, minimum, maximum) were given for the numerical variables. The normality assumptions of the numerical variables were examined using the Kolmogorov Smirnov normality test and it was observed that the variables were not normally distributed. Therefore, non-parametric statistical methods were used in the study. The differences between the two independent groups were examined using the Mann Whitney U Analysis. The relationship between two independent categorical variables was interpreted using the Chi-Square analysis. The statistical significance level in the analysis was accepted as 0.05.

RESULTS

A total of 161 stroke patients, 74 of which (46%) were female and 87 (54%) were male, were included in the study. The mean age of the patients was 70.49±15.269 years, and 97 (60.2%) patients had been diagnosed as IS, 32 (19.9%) patients had been diagnosed as HS and 32 (19.9%) patients had been diagnosed as SAH. The average length of hospitalization of the patients was 46.6±16.11 days and the GCS was 10.6±2.17. Among these patients, 92.5% had HT, 50.3% had HD, 27.3% had DM and 14.9% had dementia as comorbidity. Thirty-five (21.1%) patients had been diagnosed with delirium (**Table 1**).

There were significant differences between the patients with and without delirium in terms of age, infection status, and the length of hospitalization. Accordingly, the ages of the patients who had developed delirium were significantly lower than those who had not ($p=0.046$). The length of hospitalization of patients who had developed delirium was significantly longer and the rate of infection was significantly higher than patients who had not developed delirium ($p=0.003$, $p<0.001$) (**Table 2**).

Table 1. Demographic characteristics of stroke patients

(n=161)	Mean	Standard Deviation
Age	70.49	15.269
Length of hospitalization	46.62	16.119
GCS	10.68	2.172
	n	**%**
Gender		
Female	74	46.0
Male	87	54.0
Diagnosis		
IS	97	60.2
HS	32	19.9
SAH	32	19.9
Dementia		
Present	24	14.9
Absent	137	85.1
DM		
Present	44	27.3
Absent	117	72.7
HT		
Present	149	92.5
Absent	12	7.5
HD		
Present	81	50.3
Absent	80	49.7
Delirium		
Present	35	21.7
Absent	126	78.3
Discharge Condition		
Exitus	29	18.0
Alive	132	82.0

GCS: Glasgow coma scale, IS: Ischemic stroke, HS: hemorrhagic stroke, SAH: Subarachnoid hemorrhage, DM: Diabetes Mellitus, HT: Hypertension, HD: Heart Disease

Table 2. Evaluation of the relationship between the delirium status and the variables

	Delirium				Chi-square	p
	Present		Absent			
	n	%	n	%		
Gender						
Female	16	45.7	58	46.0	0.001	0.973
Male	19	54.3	68	54.0		
Diagnosis						
IS	17	48.6	80	63.5	5.852	0.054
HS	6	17.1	26	20.6		
SAH	12	34.3	20	15.9		
Dementia						
Present	8	22.9	16	12.7	2.228	0.135
Absent	27	77.1	110	87.3		
DM						
Present	9	25.7	35	27.8	0.059	0.809
Absent	26	74.3	91	72.2		
HT						
Present	33	94.3	116	92.1	0.006	1.000
Absent	2	5.7	10	7.9		
HD						
Present	13	37.1	68	54.0	3.102	0.078
Absent	22	62.9	58	46.0		
Infection						
Present	22	62.9	29	23.0	20.089	0.000
Absent	13	37.1	97	77.0		
Discharge Condition						
Exitus	7	20.0	22	17.5	0.120	0.729
Alive	28	80.0	104	82.5		
	Median	**Min.-Max.**	**Median**	**Min-Max.**	**Z**	**p**
Age	68.0	44-90	76.0	20-94	-1.995	0.046
GCS	10.0	7-15	10.0	7-15	-0.462	0.644
Length of hospitalization	47.0	9-257	31.0	7-257	-2.953	0.003

GCS: Glasgow coma scale, IS: Ischemic stroke, HS: Hemorrhagic stroke, SAH: Subarachnoid hemorrhage, DM: Diabetes Mellitus, HT: Hypertension, HD: Heart disease

There were significant differences between the patients with and without delirium in levels of glucose, creatinine, sodium, ALT, and albumin. There was a statistically significant relationship between the development of delirium and the PEG status. (p=0.015) While the glucose, creatinine and ALT levels of patients who had developed delirium were significantly higher than those without delirium, their Na and albumin levels were significantly lower. The proportion of patients with PEG was significantly lower among patients with delirium (p=0.0015) (**Table 3**).

There were significant differences between the patients with and without delirium the use of anticholinergics, narcotic analgesics, antiepileptics, and antipsychotics. Accordingly, the rate of anticholinergic, narcotic analgesic, antiepileptic and antipsychotic users among patients with delirium was significantly higher than those without delirium (p=0.003, p< 0.001, p=0.004, p<0.001) (**Table 4**).

Table 3. Evaluation of the relationship between the delirium status and laboratory parameters and PEG

	Delirium				Z	p
	Present		Absent			
	Median	Min.-Max.	Median	Min.-Max.		
Glucose	119.0	79-189	98.5	74-200	-2.989	0.003
Urea	23.0	0.6-64	18.0	0.2-62	-1.929	0.054
Creatinine	0.6	0.2-4.1	0.5	0.1-3.5	-2.869	0.004
K	3.9	2.9-4.9	3.9	2.3-5.4	-1.064	0.287
Na	134.0	128-143	138.0	130-147	-3.777	0.000
AST	21.0	9-66	18.0	5-44	-1.001	0.317
ALT	20.0	6-71	15.0	2-73	-2.751	0.006
Albumin	2.5	1.6-3.9	2.8	1.6-4.1	-3.561	0.000
	n	**%**	**n**	**%**	**Chi-square**	**p**
PEG						
Present	20	57.1	98	77.8	5.958	0.015
Absent	15	42.9	28	22.2		

PEG Percutaneous Endoscopic Gastrostomy, K: Potassium, Na: Sodium, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase

Table 4. Evaluation of the relationship between the delirium status and medication use

	Delirium				Chi-square	p
	Present		Absent			
	n	%	n	%		
Anticholinergic						
Present	11	31.4	14	11.1	8.620	0.003
Absent	24	68.6	112	88.9		
Narcotic Analgesic						
Present	17	48.6	5	4.0	46.191	0.000
Absent	18	51.4	121	96.0		
Antiepileptic						
Present	21	60.0	42	33.3	8.178	0.004
Absent	14	40.0	84	66.7		
Antipsychotic						
Present	13	37.1	13	10.3	14.556	0.000
Absent	22	62.9	113	89.7		

DISCUSSION

Delirium is a temporary neurocognitive disorder characterized by cognitive, psychomotor and behavioral symptoms, and it is a common complication after stroke.[13] In our study, we detected delirium in 35 (21.1%) of stroke patients followed in palliative care. In their study, Farhaan S. Vahidy and colleagues found that the rate of delirium was higher in HS patients (ICH: 10.0%, SAH: 9.8%) than in IS patients (7.0%).[14] In our study, the delirium rates in palliative care were higher in HS patients (HS: 18.5%, SAH: 37.5%) than in IS patients (17.5%), but this did not create a statistically significant difference. (p=0.054)

Previous studies have shown that advanced age, infection and dementia pose a high risk of developing delirium after a stroke.[15] In the patients we followed in palliative care who developed delirium after a stroke, the infection rate was significantly high, and their average age was significantly low. Advanced age (≥65) has been shown as a risk for delirium in many studies.[14] Caeiro et al.[16] identified the average age as 63.6 in stroke patients who developed delirium. In our study, although the mean age of patients with delirium was 66.6, it was considered to be low when compared with patients without delirium. We have thought that admission of some poststroke patients to the palliative care in the advance stage of the disease might be a factor acting on the difference in the mean age.

It was previously shown that the duration of hospitalization and mortality increased in patients who developed delirium after a stroke and that delirium negatively affected the prognosis.[17] In our study, the length of hospitalization was significantly longer in patients with stroke under our follow-up in palliative care, but there was no significant difference in the exitus rates. Similarly, Nydahl et al.[18] showed that complication rates increased, but mortality did not increase in patients with delirium that they followed in the primary stroke unit.

In their hospital-based study, Khurana and colleagues[19] showed that the second major risk factor for delirium after sepsis and infection was metabolic abnormalities. The glucose, creatinine and ALT levels were significantly higher, and the Na and albumin levels were significantly lower in patients with stroke who developed delirium, whom we followed in palliative care. In their study, Kotfis et al.[20] found that acute renal failure and impaired glucose tolerance posed a high risk of delirium development after a stroke, and that AST and creatinine values were significantly higher in patients with delirium. We identified that the PEG rate was significantly low in patients who developed delirium. We thought that this result might have been be due to the decrease in delirium development through use of a PEG, which provides a partial reduction of nutritional problems in patients with stroke followed-up in palliative care.

Medications are an increasingly common precipitant of delirium as well as other neuropsychiatric adverse effects, especially in the elderly and other patients with altered pharmacokinetics and pharmacodynamics.[21] Opioids, anticholinergics, anxiolytics, antipsychotics, antiepileptics and steroids are among the medications that most frequently cause delirium.[22] Anticholinergic agents are commonly used for the treatment of several poststroke disorders including urinary bladder problems, spasticity, depression, and pain. The effects of medications on the development of delirium in stroke patients have previously been studied in a limited number of studies, and anticholinergics have been shown to increase the risk of delirium.[16,23] In our study, we identified that the use of anticholinergics, narcotic analgesics, antiepileptics and antipsychotics was significantly high among patients with stroke who developed delirium, who had been under follow-up in our palliative care.

This study had several limitations: First, the patients included in the study had not been routinely screened for delirium; they had been accepted as delirium after evaluation by the psychiatry department. We think that some patients, particularly those who could have been diagnosed as hypoactive delirium during their clinical follow-up may have been omitted. Secondly, the etiology of delirium is multifactorial and has not been fully clarified. Location and size of the stroke lesion can be related to the risk of delirium; therefore, the lack of analysis of such a relationship is included in the limitations of this study.

CONCLUSION

Delirium is a complication that we commonly encounter, both in the acute period and during palliative care follow-up, in patients with stroke. In our study, we showed that age, infection, metabolic disorders and medications affected the development of delirium and the length of stay in palliative care in patients with stroke. We think that determining and managing the risk factors for delirium development in stroke patients followed-up in palliative care will decrease the morbidity of the patients and improve their quality of life, and that further studies on this topic are needed.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital Ethics Committee (Date: 08.07.2020, Decision No:2020-07/682).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, (Fifth Edition ed). Arlington:American Psychiatric Association, 2013.
2. Creutzfeldt CJ, Longstreth WT, Holloway RG. Predicting decline and survival in severe acute brain injury:the fourth trajectory. BMJ. 2015;351:h3904.
3. McManus J, Pathansali R, Stewart R, Macdonald A, Jackson S. Delirium Post-Stroke. Age Ageing. 2007;36(6):613-8.
4. Inouye SK, Westendorp RGJ, Saczynski JS. Delirium in Elderly People. Lancet. 2014;383(9920):911-22.
5. Holloway RG, Arnold RM, Creutzfeldt CJ, et al. Palliative and end-of-life care in stroke:a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45:1887-916.
6. Holloway RG, Ladwig S, Robb J, Kelly A, Nielsen E, Quill TE. Palliative Care Consultations in Hospitalized Stroke Patients. J Palliat Med. 2010;13(4):407-412.
7. Eastman P, McCarthy G, Brand CA, Weir L, Gorelik A, Le B. Who, Why and When:Stroke Care Unit Patients Seen by a Palliative Care Service Within a Large Metropolitan Teaching Hospital. BMJ Support Palliat Care. 2013;3(1):77-83.
8. Patel MB, Bednarik J, Lee P, et al. Delirium Monitoring in Neurocritically Ill Patients:A Systematic Review. Critical care medicine. 2018;46(11):1832-41.
9. Naidech AM, Beaumont JL, Rosenberg NF, et al. Intracerebral hemorrhage and delirium symptoms. Length of stay, function, and quality of life in a 114-patient cohort. American journal of respiratory and critical care medicine. 2013;188(11):1331-7.
10. Hosie A, Davidson PM, Agar M, Sanderson CR, Phillips J. Delirium prevalence, incidence, and implications for screening in specialist palliative care inpatient settings:a systematic review. Palliat Med. 2013;27(6):486-98.
11. 11.Kim H, Chung S, Ho Joo Y, Lee JS. The major risk factors for delirium in a clinical setting. Neuropsychiatr Dis Treat. 2016;12:1787-93.
12. Shi Q, Warren L, Saposnik G, MacDermid JC. Confusion assessment method:a systematic review and meta-analysis of diagnostic accuracy. Neuropsychiatr Dis Treat. 2013;9:1359-70.
13. Langhorne P, Stott DJ, Robertson L, et al. Medical complications after stroke:A multicenter study. Stroke. 2000;31(6):1223-29.
14. Vahidy FS, Bambhroliya AB, Meeks JR, et al. In-hospital outcomes and 30-day readmission rates among ischemic and hemorrhagic stroke patients with delirium. PLoS One. 2019;14(11):e0225204.
15. Simone MJ, Tan ZS. The Role of Inflammation in the Pathogenesis of Delirium and Dementia in Older Adults:A Review. CNS Neurosci Ther. 2011;17(5):506-13.
16. Caeiro L, Ferro JM, Claro MI. Delirium in acute stroke:a preliminary study of the role of anticholinergic medications. Eur J Neurol. 2004;11:699-704.
17. McManus J, Pathansali R, Hassan H, et al. The course of delirium in acute stroke. Age and Aging. 2009;38:385-9
18. Nydahl P, Bartoszek G, Binder A, et al. Prevalence for delirium in stroke patients:A prospective controlled study. Brain Behav. 2017;7(8):e00748.
19. Khurana V, Gambhir IS, Kishore D. Evaluation of delirium in elderly:a hospital-based study. Geriatr Gerontol Int. 2011;11:467-73.
20. Kotfis K, Bott-Olejnik M, Szylińska A, Listewnik M, Rotter I. Characteristics, Risk Factors And Outcome Of Early-Onset Delirium In Elderly Patients With First Ever Acute Ischemic Stroke-A Prospective Observational Cohort Study. Clin Interv Aging. 2019;14:1771-82.
21. Bush SH, Tierney S, Lawlor PG. Clinical Assessment and Management of Delirium in the Palliative Care Setting. Drugs. 2017;77(15):1623-43.
22. Jackson N, Doherty J, Coulter S. Neuropsychiatric Complications of Commonly Used Palliative Care Drugs. Postgrad Med J. 2008;84(989):121-6
23. Gustafson Y, Olsson T, Eriksson S, Asplund K, Bucht G. Acute confusional states (delirium) in stroke patients. Cerebrovasc Dis. 1991;1:257-64.