

# Six-Month Follow-Up of Delirium Patients: Evaluation of Anxiety, Depression, Cognition, Functioning, and Mortality

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## Abstract

**Introduction:** This study sought to monitor the anxiety and depression symptoms, cognition, functioning, and mortality of inpatients diagnosed with delirium and to compare the results with those of a control group comprised of inpatients without delirium.

**Materials and methods:** The study group consisted of 50 inpatients with delirium, while the control group comprised 50 inpatients from the same clinic who did not have delirium. A sociodemographic questionnaire and the Delirium Rating Scale (DRS), Hospital Anxiety and Depression Scale (HADS), Mini Mental State Examination (MMSE), and Global Assessment Scale (GAS) were used for data collection purposes.

**Results:** The MMSE and GAS scores of the delirium group were significantly lower than those of the control group at the first assessment. In addition, the increase seen in the MMSE scores of the delirium group over time was significant. At the three- and six-month follow-up assessments, the mortality rate of the delirium group was higher than that of the control group. Moreover, the mean survival duration of the delirium group at the three- and six-month assessments was significantly shorter than that of the control group.

**Conclusion:** The findings showed that the delirium patients experienced deterioration in their cognition and functioning in the short term. Furthermore, the findings revealed life expectancy to be shortened in the delirium patients. To verify and extend the present findings, longitudinal studies involving larger sample sizes and longer follow-up periods are required.

**Keywords:** Delirium; anxiety; depression; cognitions; functioning; mortalities.

## Introduction

Delirium is a temporary organic mental syndrome characterized by the sudden onset of a deterioration in consciousness, attention, and the sleep-wake cycle (1). Delirium has been found to occur in 26%–44% of all hospital admissions, while it has been reported to have a prevalence of up to 80% in critically ill patients (2). Although previously considered a transient syndrome, recent studies have determined that delirium and its symptoms often persist for up to one year (3,4). For instance, in a study involving inpatients with delirium who were followed up for 12 months after discharge, the participants were found to have a 62% increased risk of mortality and to survive for an average of 47.5 days less than patients without delirium (5). In recent years, there has been increasing research interest in the effects of delirium on healthcare outcomes such as the prolongation of hospital stay, increase in healthcare costs, decrease in quality of life, short-

and long-term mortality rates, and long-term cognitive impairment (6). Patients who have previously experienced delirium tend to experience more cognitive problems than patients who have not experienced delirium. Overall, the total self-reported cognitive functioning of patients who have had delirium has been found to be significantly impaired (7). The cognitive impairment associated with delirium was previously thought to be reversible following the resolution of the underlying pathology, although a growing body of evidence suggests that delirium may lead to both long-term cognitive impairment and a worse prognosis (8). In addition, it has been found that delirium is associated with functional decline and the need for prolonged rehabilitation, nursing home placement, and assistance with self-care and daily activities such as dressing and shopping in the short and long term (9,10). The present study sought to assess inpatients with

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delirium over a six-month period following their discharge from hospital. The patients were evaluated in terms of their cognition, mortality, functioning, and anxiety and depression symptoms. In addition, the results were compared with the results of the six-month follow-up of a control group comprised of inpatients without delirium. It was hypothesized that delirium would have an adverse effect on the trajectory of inpatients with delirium, who would exhibit worse outcomes than the control group with regard to the variables of interests.

## Materials and Methods

**Study design:** This study was conducted between October 2015 and March 2016 after approval was granted by the medical ethics committee of Atatürk University, Faculty of Medicine. Ethics Committee approval was obtained on 17.09.2015 with the decision numbered 15 of the session numbered 6. The study included 50 delirium patients hospitalised in internal medicine departments, surgical medicine departments and intensive care units of the hospital who consulted to the psychiatry department. The delirium group had been diagnosed with delirium according to the criteria specified in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5). All the diagnoses of delirium were made by the first author of the present paper, who was a senior psychiatry resident in the hospital's psychiatry department. Patients who were diagnosed with delirium as a result of consultation evaluation and met the inclusion criteria were included in the study. The control group was composed of 50 inpatients randomly selected from other patients who were hospitalised in the same clinic with delirium patients and who met the inclusion criteria. The inclusion criteria were determined as being 18 years of age or older and accepting to participate in the study after the patients and their relatives were informed. Exclusion criteria were the presence of psychiatric disorder, mental retardation or dementia and refusal of the patient or relatives to participate in the study. The presence of previous psychiatric disease history was evaluated according to the information obtained from the patients and their relatives and the medical records obtained. Since the patient group was consulted in the psychiatry department, a detailed diagnostic interview was performed. In the control group, the presence of psychiatric illness was excluded by anamnesis, examination of medical records and mental status examination. As a result of these evaluations, those who had

psychiatric diseases and therefore used psychotropic drugs were excluded from the study. The sample size of this prospective study was calculated using G\*Power statistical programme (ver.3.1.9.7)\*. Accordingly, it was determined as "90 patients in total, with a minimum of 45 patients in each group" (for Study and Control groups) by taking Power (power of the test) 0.80, Effect size 0.6 (t-test effect size value range) and Type-1 error ( $\alpha$ ) 0.05. However, in order to secure the number of samples and to keep the Power value high, the number of samples was increased and a total of 100 samples (50 samples in each group) were used. The Power (power of the test) recalculated according to this sample number increased to 83%. A sociodemographic questionnaire and the Delirium Rating Scale (DRS), Hospital Anxiety and Depression Scale (HADS), Mini Mental State Examination (MMSE), and Global Assessment Scale (GAS) were administered to the participants for data collection purposes. HADS, MMSE and GAS which were applied to delirium patients in the first assessment, were applied after the delirium symptoms of the patients improved. Therefore, patients with delirium were examined daily by the researcher until their symptoms improved. At the three-month or six-month follow-up assessments, the participants were contacted by calling patients or their relatives by telephone. Those who were alive and agreed to come to the hospital for follow-up were re-evaluated by the researcher.

### Clinical measures:

**Sociodemographic data form:** The researches developed a sociodemographic data form to ascertain individuals' characteristics including their age, gender, marital status, education level and history of psychiatric and physical illness in both their personal and familial backgrounds.

**Delirium rating scale:** The DRS was used to diagnose delirium in this study. It consists of ten questions that are answered using four-point Likert-type measurement scales. The total score is between 0–30, while the cut-off point is 11/12. The Turkish version of the scale was used in this study (11).

**Mini mental state examination:** The MMSE was used to evaluate the orientation, recording memory, attention, calculation, recall, and language domains of cognition. It consists of 21 items. There are separate forms available for literate and illiterate individuals. The validity and reliability of the examination with regard to the diagnosis of mild dementia among a Turkish population were demonstrated by Güngen et al. in 2002 (12).

**Table 1:** Sociodemographic characteristics of the depression and control groups

		Delirium Group				Control Group	
		(N:50)		(N:50)		Chi-square	P
		N	%	N	%		
Gender	Female	18	36.0%	22	44.0%	0.667	0.414
	Male	32	64.0%	28	56.0%		
Education status	Illiterate	19	38.0%	16	32.0%	1.843	0.389
	Primary school graduate	21	42.0%	21	42.0%		
	Secondary school graduate	5	10.0%	4	8.0%		
	High school graduate	4	8.0%	4	8.0%		
	University graduate	1	2.0%	5	10.0%		
Marital status	Single	4	8.0%	6	12.0%	1.843	0.389
	Married	34	68.0%	37	74.0%		
	Divorced/Widow	12	24.0%	7	14.0%		

  

	Group							
	Delirium Group			Control Group			Z	P
	N	Mean±std	Median (min- max)	N	Mean±std	Median (min- max)		
Age	50	65.7±16.41	68.5(19-90)	50	52.28±18.29	57.5(18-84)	-3.983	.000
Education year	50	4.18±3.86	5(0-15)	50	5.28±4.75	5(0-16)	-.899	.369

std: standart deviation

The highest score is 30, while the cut-off point for dementia is 23/24. In this study, both forms were used, depending on the education levels of the participants.

**Hospital anxiety and depression scale:** The HADS is a self-report scale consisting of 14 questions. Half the questions check for the symptoms of anxiety, while the remainder check for the symptoms of depression. Responses are given using four-point Likert-type measurements scales, with the scores ranging from 0–3. In a study conducted in Turkey, the cut-off score was determined to be 10/11 for the anxiety subscale and 7/8 for the depression subscale (13).

**Global assessment scale:** The GAS was developed in 1976 by Endicott et al. (14). Based on a scale ranging from 0–100, it evaluates a patient’s general well-being and functioning using variables such as disease symptoms, social and professional functioning, and ability to cope with problems.

**Statistical analyses:** The normal distribution of the continuous variables was assessed using the Shapiro-Wilk test. The independent samples t-test was used for comparisons between the two groups when the normal distribution condition was satisfied, while the Mann-Whitney U test was used when the difference was not available. The repeated measures analysis of variance (ANOVA) test was used when the normal distribution

condition was met in relation to the comparison of the over-dependent group variables, whereas the Friedman test was used otherwise. The comparison between the categorical variables was performed using the Chi-square test and Fisher’s exact test. The analysis of covariance (ANCOVA) test was used to perform multiple comparisons. The survival effects of the groups were assessed by means of a survival analysis. Statistical significance was considered to be  $p < 0.05$ .

## Results

Of the delirium inpatients, 48% ( $n = 24$ ) were evaluated in the hospital’s internal medicine departments, 32% ( $n = 16$ ) in the surgical medicine departments, and 20% ( $n=50$ ) in the intensive care units. The majority of participants in both the delirium group and the control group were male ( $n = 32$  [64%] and  $n = 28$  [56%], respectively). The mean age of the participants in the delirium group was  $65.7 \pm 16.41$  years, while in the control group it was  $52.28 \pm 18.29$  years. Thus, the mean age of the participants in the control group was significantly lower than that of the participants in the delirium group ( $p<0.001$ ) (Table 1). At the three-month follow-up assessment, 10 patients from the delirium group and 16 from the control group were evaluated, while at the six-month assessment, 11 patients from the delirium group and 16 from the control

**Table 2:** 3rd month mean survival days

Estimate	Std. Error	Mean <sup>a</sup>		Median				
		95% Confidence Interval		95% Confidence Interval				
		Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound	
Delirium Group	48.200	5.407	37.603	58.797	43.000	25.927	0.000	93.817
Control Group	81.520	2.818	75.997	87.043				
Overall	64.860	3.474	58.051	71.669				
		Chi-Square	df	Sig.				
LogRank (Mantel-Cox)		21.934	1	.000				

<sup>a</sup>Estimation is limited to the largest survival time if it is censored.  
 Test of equality of survival distributions for the different levels of groups.  
**df:** Degree of freedom; **sig:**Significance, **Std. Error:** Standart Error

**Table 3:** 6th month mean survival days

Group	Estimate	Std. Error	Mean <sup>a</sup>		Median			
			95% Confidence Interval		95% Confidence Interval			
			Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
DeliriumGroup	82.920	11.181	61.006	104.834	43.000	25.927	0.000	93.817
Control Group	150.460	7.913	134.951	165.969				
Overall	116.690	7.636	101.724	131.656				
		Chi-Square	df		Sig.			
LogRank (Mantel-Cox)		18.450	1		.000			

<sup>a</sup> Estimation is limited to the largest survival ime if it is censored.  
 Test of equality of survival distributions for the different levels of group.  
**df:** Degree of freedom; **sig:** Significance, **Std. Error:** Standart Error

**Table 4:** MMSE scores and change over time

	Group							
	Delirium Group			Control Group			Z	P
	N	Mean±std	Median (min-max)	N	Mean±std	Median (min-max)		
MMSE score, 0th month	34	19.27±6.63	20.5(7-29)	50	25.38±4.81	27(11-30)	-4.579	.000
MMSE score, 3rd month	10	23.8±5.73	25(14-30)	16	26.5±4.00	28(15-30)	-.961	.337
MMSE score, 6th month	11	24.37±5.28	25(16-30)	16	27.13±2.78	28(21-30)	-1.026	.305
Chi-square			13.152		1.938			
P			0.001		0.380			

**MMSE:** Mini Mental State Examination

delirium group and 18% (n = 9) of the control group had died. In addition, at the three-month assessment, the mean survival duration of the delirium group was found to be 48.2 ± 5.41 days, while it was found to be 81.52 ± 2.82 days for the control group. The mean survival duration of the control group was significantly higher than that of the delirium group (p<0.001) (Table 2). At the six-month follow-up assessment, 62% (n = 31) of the delirium group and 24% (n = 12) of the control group were found to have died. Moreover, also at the six-month assessment, the mean survival duration of the delirium group was determined to be 82.92 ± 11.18 days, while it was 150.46 ± 7.91

days for the control group. Thus, the mean survival duration of the control group was significantly higher than that of the delirium group (p<0.001) (Table 3). As a significant difference between the mean ages of the control and delirium groups was identified, a covariance analysis was applied to determine the effect of age on both the first-day MMSE score and the survival duration. It was found that the age variable had a confounding effect (p<0.001) on the MMSE score on the first day of the study, whereas it had no confounding effect on the survival duration (p = 0.321). During the participants' first assessment, the mean MMSE score of the delirium group was found to be

19.27 ± 6.6, while it was determined to be 25.38 ± 4.81 for the control group, which revealed that the mean score of the control group was significantly higher than that of the delirium group (p<0.001) (Table 4). However, there was no significant difference observed between the delirium and control groups in terms of the mean MMSE scores at the second and third assessments. In the delirium group, the mean MMSE score was found to be 19.27 ± 6.63 at the first follow-up assessment, 23.8 ± 5.73 at the three-month assessment, and 24.37 ± 5.28 at the six-month assessment, with the increase in the test scores over time being significant (p = 0.001). In the control group, the mean MMSE score did not

differ significantly over time. There was no significant difference observed between the delirium group and the control group with regard to the anxiety and depression subscale scores for the HADS at the first, three-month or six-month follow-up assessments (Tables 5). The median GAS value of the delirium group was 7.5 (4–10) at the first assessment, while it was 8.5 (5–10) for the control group. Thus, the control group had significantly higher GAS scores than the delirium group at the initial assessment (p = 0.004). At the three- and six-month assessments, the median GAS values of the delirium and control groups did not differ significantly.

**Table 5:** HAD Scale, anxiety subscale scores between groups and change over time, HAD Scale, depression subscale scores between groups and change over time, GAS scores and change over time

	Group							Z	P
	Delirium Group			Control Group					
	N	Mean±std	Median (min-max)	N	Mean±std	Median (min-max)			
HAD scale, Anxiety Score, 0th month	34	3.80±3.891	3(0-15)	50	3.82±4.374	2.50(0-19)	-0.214	.831	
HAD scale, Anxiety Score, 3rd month	10	3.4±3.658	3,5(0-11)	16	5.31±6.426	3(0-18)	-0.326	.744	
HAD scale, Anxiety Score, 6th month	11	3.73±4.292	3(0-11)	16	3.81±3.655	3(0-11)	-0.375	.708	
Chi-square			3.600			1.697			
P			0.165			0.428			

  

	Group							Z	P
	Delirium Group			Control Group					
	N	Mean±std	Median (min-max)	N	Mean±std	Median (min-max)			
HAD scale, Depression Score, 0th month	34	4.21±4.443	3(0-17)	50	2.92±3.579	1(0-14)	-1.354	.176	
HAD scale, Depression Score, 3rd month	10	5.3±6.413	2(0-19)	16	3.19±4.339	0,5(0-13)	-1.180	.238	
HAD scale, Depression Score, 6th month	11	3.91±4.989	2(0-13)	16	2.63±3.845	0(0-10)	-0.943	.346	
Chi-square			4.000			3.583			
P			0.135			0.167			

  

	Group							Z	P
	Delirium Group			Control Group					
	N	Mean±std	Median (min-max)	N	Mean±std	Median (min-max)			
GAS score, 0th month	34	7.53±2	7.5(4-10)	50	8.5±1	8.5(5-10)	-2.850	.004	
GAS score, 3rd month	10	7.9±2	8.5(5-10)	16	8.38±2	9(5-10)	-0.551	.581	
GAS score, 6th month	11	8.1±2	8(6-10)	16	9±1	9.5(6-10)	-1.276	.202	
Chi-square			1.520			2.375			
P			0.468			0.305			

**HAD scale:** Hospital Anxiety and Depression scale

**GAS:** Global Assessment Scale

In addition, no significant difference was found in terms of the GAS scores within both the delirium

group and the control group at the first, three-month, and six-month assessments (Table 5).

## Discussion

The present study found the mortality rate of the delirium group to be higher than that of the control group throughout the six-month follow-up period. Furthermore, the mean survival duration of the delirium group was significantly shorter than that of the control group. The cognition and functioning of the delirium patients were worse than the cognition and functioning of the control group at the first assessment but not at the three- and six-month assessments. There was no difference between the groups in terms of the anxiety and depression symptom scores throughout the six-month follow-up period. Delirium is known to be associated with high mortality rates. However, it remains unclear if the relationship between delirium and mortality is related to the pathophysiology of delirium or to its secondary complications, such as infection, falls, and non-compliance with treatment. In the majority of studies that have sought to assess the relationship between mortality and delirium, the mortality rates of elderly patients who had been admitted to intensive care units were evaluated (15,16). Only a limited number of studies investigated the mortality rate among inpatients with delirium who had been admitted to psychiatry departments. In line with the present results, Tennen et al. (17) performed a one-year follow-up of patients who required psychiatry consultations and found that delirium was the only psychiatric disorder associated with one-year mortality. In a study in which patients with delirium were followed up for six months, the mortality rate of the delirium patients was found to be 42.9%, which was significantly higher than the rate of the patients without delirium (9.6%) (18). Moreover, in a study in which delirium patients were followed up for one year, the one-year mortality rate was determined to be 63.3%, and delirium was found to be associated with high mortality at the one-, six-, and twelve-month assessments (19). In line with these prior studies, in the present study, the mortality rate was higher in the delirium group. The three-month mortality rate of the delirium patients was 60%, while the six-month mortality rate was 62%. Additionally, the mean survival duration of the control group was significantly higher than that of the delirium group. Mortality rates vary among studies. The number of samples, methods of evaluating delirium, and differences in medical diseases may explain such differences. In the present study, the mean MMSE score of the delirium group was significantly lower than that of the control group at the first assessment. In addition, the increase in

the MMSE score in the delirium group over time was significant, which was likely due to the temporary deterioration caused by delirium. Indeed, it has been established that delirium is generally a temporary condition that only rarely becomes chronic. While the underlying pathophysiology of delirium is not yet fully understood, some hypothesize that its mechanism is similar to the mechanisms of the neurodegenerative processes involved in Alzheimer's disease and other types of dementia. One mechanism that predisposes a person to delirium is central cholinergic insufficiency (20). Aside from the fact that cognitive impairment is a risk factor for the development of delirium, there is evidence to suggest that delirium increases the risk of dementia in those without cognitive impairment and also accelerates cognitive impairment in patients with Alzheimer's disease (21). In light of such data, the relationship between delirium and cognitive impairment is thought to be bidirectional. In this study, the basal cognition levels of the delirium group prior to the diagnosis of delirium were unknown. The MMSE was applied to the delirium group immediately after the improvement of their delirium symptoms, while it was applied to the control group during the first assessment. At the initial follow-up assessment (the day the delirium symptoms were noted to be severely alleviated), the delirium group's MMSE scores were significantly lower than those of the control group. In addition, delirium itself was considered to be the main contributing factor to the difference in the initial MMSE scores observed between the two groups. Moreover, an increase in the MMSE scores in both groups was observed at the three- and six-month assessments. However, the increase in the delirium group was significant, whereas it was not significant in the control group. Although delirium is known to be associated with long-term cognitive impairment, the cognitive improvement seen in the delirium group in this study was thought to be associated with the delirium patients' baseline cognition levels prior to the onset of delirium as well as to the comparison with their cognition levels immediately after the delirium. Interestingly, there was no significant difference noted between the two groups in terms of the MMSE scores at the three- and six-month assessments. Some studies have shown the symptoms of depression to be predictive factors with regard to delirium (22,23). Moreover, major depressive disorder and delirium are thought to share certain common pathophysiological pathways, such as the limbic-

hypothalamic-pituitary-adrenal axis system, inflammatory response, and sympathetic system. In addition, Davydow (24) indicated that depression and anxiety may result from delirium, meaning that there could be a bidirectional relationship between delirium and affective disorders. It has been observed that delirium generally gives rise to depressive symptoms, although studies investigating the relationship between delirium and anxiety symptoms have reported conflicting results (25-28). While no significant differences in terms of the anxiety and depression scores were observed between the two groups in this study, the depression scores of the delirium group were higher than those of the control group, whereas the anxiety scores of the two groups were similar. One negative consequence of delirium involves a decrease in short- and long-term functioning (9,29). In fact, prior studies have shown delirium to be associated with decreased functioning throughout the follow-up period (18,30). At the first day of follow-up in the present study, the GAS scores of the delirium group were found to be significantly lower than those of the control group, which may have been related to the worse general medical condition of the delirium patients as well as to the negative effect of delirium on short-term functioning. In this study, in accordance with the results of other studies, while not statistically significant, the delirium group's functioning scores at the three- and six-month assessments were lower than those of the control group. It is considered that the low functioning and high mortality rates seen in relation to the delirium patients might be due to factors such as physical diseases and environmental differences. Thus, these factors might be predisposing factors when it comes to delirium. The strengths of our study include the fact that it was a six-month follow-up study and that all evaluations were conducted by the same researcher. In addition, in our study, delirium cases were evaluated in many areas, including anxiety and depression symptoms, cognition, functioning and mortality rates, and we tried to contribute to the literature in these areas.

**Study limitations:** It must be noted that this study had a number of limitations. First, although the effect of different ages on all the evaluations was controlled for by means of further statistical analyses, the mean age of the delirium group was higher than that of the control group, which could have contributed to the difference seen in the MMSE scores between the groups at the first follow-up assessment as well as to the low functioning in the delirium group. Older age is

known to be a risk factor for delirium. Yet, as the results of the two groups at the three- and six-month assessments were similar, it is considered that age may have an increasing effect on the development of delirium but a negligible effect on measurements such as cognition, depression and anxiety symptoms, and functioning during the post-delirium period. None of the patients in this study had chronic delirium. This supports the findings that delirium had temporary effects on cognition and functioning but not on anxiety and depression symptoms in the short term and at the six-month follow-up assessment. Another limitation concerns the fact that at the three- and six-month assessments, only a small number of patients from the delirium and control groups were reached. In addition, both groups' cognitive and functioning levels prior to the delirium assessment were unknown. This may have led to different results between the two groups. Another limitation of our study is that the primary diseases of patients with delirium may also have an effect on survival times.

## Conclusion

The findings of this study revealed that delirium patients experienced a deterioration in their cognition and functioning in the short term. Moreover, delirium patients were found to have a reduced life expectancy. Therefore, healthcare teams should be mindful of the risk assessment, prevention strategies, and early diagnosis and treatment of delirium. Longitudinal studies involving larger sample sizes, longer follow-up periods, and age-matched control groups are required to validate and extend the present findings. For further studies, it is recommended to exclude the effect of factors such as physical diseases and medications that may have an effect on mortality and cognitive functions in the delirium group.

**Ethical approval:** Ethics Committee approval was obtained from Atatürk University Faculty of Medicine Clinical Research Ethics Committee on 17.09.2015 with the decision numbered 15 of the session numbered 6.

**Conflict of interest:** The authors have no conflict of interest related to this study.

**Financial support:** No financial support was received for this study.

**Author contributions:** Concept (T.Ü., H.Ö.), Design (H.Ö., E.F.A.), Supervision (H.Ö.), Financing (T.Ü.), Materials (T.Ü.), Data Collection and/or Processing (T.Ü.), Analysis and/or Interpretation (H.Ö.), Literature Review (T.Ü.), Writing - Original Draft (T.Ü.), Writing - Review

and Revision (H.Ö., E.F.A.), Critical Review (H.Ö., E.F.A.), Software and Visualisation Support (E.F.A.)

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