Delirium in critically ill patients: Impact on long-term health-related quality of life and cognitive functioning*

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Objective: **To examine the impact of delirium during intensive care unit stay on long-term health-related quality of life and cognitive function in intensive care unit survivors.**

Design: **Prospective 18-month follow-up study.**

Setting: **Four intensive care units of a university hospital.**

Patients: **A median of 18 months after intensive care discharge, questionnaires were sent to 1,292 intensive care survivors with (n = 272) and without (n = 1020) delirium during their intensive care stay.**

Measurements and Main Results: **The Short Form-36v1, checklist individual strength-fatigue, and cognitive failure questionnaire were used. Covariance analysis was performed to adjust for relevant covariates. Of the 915 responders, 171 patients were delirious during their intensive care stay (median age 65 [interquartile range 58–85], Acute Physiology and Chronic Health Evaluation II score 17 [interquartile range 14–20]), and 745 patients were not (median age 65 [interquartile range 57–72], Acute Physiology and Chronic Health Evaluation II score 13 [interquartile range 10–16]). After adjusting for covariates, no differences were found between delirium and nondelirium survivors on the Short Form-36 and checklist individual strength-fatigue. However, survivors who had suffered from delirium reported that they made significantly more social blunders, and their total cognitive failure questionnaire score was significantly higher, compared to survivors who had not been delirious. Survivors of a hypoactive delirium subtype performed significantly better on the domain mental health than mixed and hyperactive delirium patients. Duration of delirium was significantly correlated to problems with memory and names.**

Conclusions: **Intensive care survivors with delirium during their intensive care unit stay had a similar adjusted health-related quality of life evaluation, but significantly more cognitive problems than those who did not suffer from delirium, even after adjusting for relevant covariates. In addition, the duration of delirium was related to long-term cognitive problems. (Crit Care Med 2012; 40:112–118)**

KEY WORDS: cognition; critical care; delirium; health-related quality of life; intensive care

Delirium is a disorder that frequently occurs in intensive care unit (ICU) patients (1–3), and is recognized as acute brain dysfunction with changes in consciousness and cognition, which fluctuate during the day (4). This disorder is associated with serious health problems and long-term cognitive impairment (5, 6). Generally, without distinguishing between delirium and nondelirium patients, 25% to 78% of ICU patients experience cognitive impairments after discharge from the ICU (7), emphasizing the need for more attention in the period following critical illness. There is a growing interest in health-related quality of life (HRQoL) after ICU discharge (8–13). HRQoL questionnaires are usually subdivided into dimensions relating to physical, mental, and social functioning. It is recognized that the value of measurements of cognitive functioning with a general HRQoL questionnaire is limited in this setting, and specific surveys measuring patients cognitive functioning, such as the validated self-reporting cognitive failure questionnaire (CFQ) (14), have been developed.

Only two studies have examined the impact of delirium on HRQoL in ICU survivors (6, 13). These studies were rather small, relatively short with a maximum follow-up of 3 and 12 months, and no analyses of the delirium subtypes were performed (6, 13). A significant difference between delirium and nondelirium patients in role-physical function, which mostly reflects functioning in daily activities, was reported (13), however, no correction for disease severity was performed (13). This implies that these findings could be the result of an epiphenomenon. The duration of delirium during patients' ICU stay was associated with their observed impaired cognitive performance (6). Little is known about the long-term (>1 yr) effects of delirium on aspects of the HRQoL in this specific group of patients. In addition, it is unknown if there are differences in HRQoL (including cognitive function) for subtypes of delirium (3) or if there is a correlation between the duration of delirium and HRQoL.

Therefore, the aim of this study was to compare the HRQoL, including self-reported cognitive functioning, in ICU survivors with delirium during their ICU stay with those that did not suffer from delirium, after a median of 18 months

*See also p. 319.

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Mr. van den Boogaard carried out the study, the statistics and drafted the manuscript. Ms. Schoonhoven and Dr. Pickkers were involved in the design, supervised the study and helped to draft the manuscript. Drs. Evers, van der Hoeven, and van Achterberg supervised the study and corrected the manuscript. All authors read and approved the final manuscript.

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after ICU discharge. Furthermore, we examined the correlations between duration of delirium and HRQoL, and if subtypes of delirium exerted different effects on HRQoL.

MATERIALS AND METHODS

Subjects

All consecutive patients admitted to the ICU of the Radboud University Nijmegen Medical Centre between February 2008 and February 2009 were screened for delirium three times a day with the confusion assessment method (CAM)-ICU (1, 15) by well-trained ICU nurses (16). In February 2010, after a median duration of 18 months after ICU discharge, we evaluated the HRQoL of the surviving patients. The regional Medical Ethical Committee approved the study (study number 2010/008) and waived the need for informed consent, since the objective of this study was to evaluate regular patient care.

Procedures

All ICU patients were included in this study except those who: were admitted for <1 day; were suffering from sustained coma in the ICU; had serious auditory or visual disorders; were unable to understand Dutch; were severely mentally disabled; were suffering from a serious receptive aphasia; or whose delirium screening was not complete during their ICU stay. Patients were diagnosed with delirium when they had at least one positive CAM-ICU screening during their complete ICU stay, as previously described (17, 18). To secure the quality of the delirium diagnosis, medical and nursing files of all patients were also screened daily for signs of delirium (19). When the files contained signs of delirium without a positive CAM-ICU screening, patients were additionally screened by a delirium expert according to the Diagnostic and Statistical Manual of Mental Disorders-IV criteria (4) to rule out false negatives and positives. In total, 17 patients (1.1%) were additionally screened this way by a delirium expert. Patients with delirium were divided into three subtypes (3): hyperactive delirium subtype with symptoms of hyperalertness and agitation (Richmond Agitation Sedation Scale + 1/+4); hypoactive subtype in which the patient is hypoalert, lethargic (Richmond Agitation Sedation Scale 0/-3); and the alternating or mixed subtype (Richmond Agitation Sedation Scale + 4/-3). This last subtype of delirium is characterized by alternating symptoms of hyperactive and hypoactive delirium.

Demographic variables as well as data of severity of illness, delirium duration, and delirium subtype of these patients were collected.

At a median 18 months after ICU discharge, an HRQoL survey was sent out to the cohort of ICU survivors. Four weeks after this, a reminder letter was sent to the nonresponders. We used three different validated instruments to measure the HRQoL. We will refer to these three tests as the HRQoL. Although there is no specific HRQoL instrument for ICU patients, recommended instruments for ICU patients are the Short Form-36 (SF-36) and the EuroQoL-5D (20). We used the validated Dutch version of the SF-36 version 1 (21), containing eight multi-item dimensions: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. Aggregated summary scores were calculated for physical and mental functioning, expressed in physical component score and mental component score, respectively. To calculate the physical component score and mental component score, we used the standardized Dutch population scores (22). In line with the SF-36 Health Survey Manual (23), missing values were imputed, and data were recoded and subsequently scored (range 0 to 100). A higher score indicates a higher level of functioning. Additionally, the shortlist of the Dutch validated checklist individual strength (CIS)-fatigue, consisting of eight questions scored on a 7-point Likert scale (24), was used. The range of the CIS-fatigue is 8 to 56, a higher score indicating more pronounced fatigue. The third instrument was the validated Dutch translation (25) of the cognitive failure questionnaire (CFQ), which is a self-reported cognitive functioning questionnaire. This questionnaire consists of 25 questions (14). The self-reported CFQ measures consist of four dimensions (26) of cognition: memory, distractibility, social blunders, and names. Each question of the CFQ was scored on a 5-point Likert scale. The total score on the CFQ ranges from 0 to 100, a higher score indicates more self-reported cognitive dysfunction. Thus, our self-reported HRQoL survey consisted of a total of 69 questions, which took an estimated 45–60 mins to answer.

To guarantee the patient's privacy, the survey was sent out anonymously and numbered. This allowed the primary and supervising investigator to match the returned survey with the patient's registry number in a separate, confidential database.

Statistical Analyses

The differences between those who suffered from delirium and nondelirium in ICU survivors were tested nonparametrically using the Mann-Whitney *U* test. Dichotomous variables were tested with the chi-square test. Since the results of our HRQoL were nonnormally distributed, log transformation of all HRQoL data was carried out successfully and the duration of delirium was divided into quartiles, resulting in normally distributed outcome measurements. The correlation between duration of delirium divided into quartiles and the log-transformed HRQoL was tested using Pearson's correlation coefficient. Significant differences in demographic variables between nondelirium and delirium patients and differences between the delirium subtypes were considered as covariates and a multivariate analysis of covariance was performed. Since there was no difference in age between delirium and nondelirium responders in our population, adjusting for age was unnecessary. In view of the explorative nature of this study, and to increase its sensitivity, no correction for multiple testing was performed.

Statistical significance was defined as a p value $< .05$. All data were analyzed using SPSS version 16.01 (SPSS, Chicago, IL).

RESULTS

At the median of 18 months before this HRQoL survey, a total of 1,613 consecutive patients who fulfilled the inclusion criteria were admitted (Fig. 1). In this group, 1,202 patients had no delirium and 411 were delirious during their ICU stay. Overall, 183 patients died, of whom 58 (5%) had not been delirious and 80 (19%) had. The hypoactive delirium subgroup had a similar number of survivors compared to the mixed subgroup, while survival was significantly higher ($p = .02$) in the hyperactive subgroup (Fig. 1), a median 18 months after ICU discharge. In total, 55 patients were admitted to the ICU more than once and 14 patients were lost to follow-up.

In total, there were 1,292 ICU survivors (Fig. 1), of whom 272 patients (21%) suffered from delirium during their ICU stay and 1,020 patients did not. In the delirious group, seven patients (3%) with a hyperactive subtype of delirium had one positive CAM-ICU screening, and 264 patients had at least two positive CAM-ICUs during their ICU stay. Median 18 months (interquartile range 15–21) after ICU discharge, a total of 915 out of the 1,292 eligible patients (71%) returned the questionnaire. Of these responders, 171 out of 272 (63%) patients suffered from delirium during their ICU stay and 744 out of 1,020 (73%) did not. Seven hundred eighty-eight survivors completed all questionnaires, 91% completed the SF-36, 98% completed the CIS-fatigue, and 97% answered all the questions of the CFQ. The demographic data and illness-

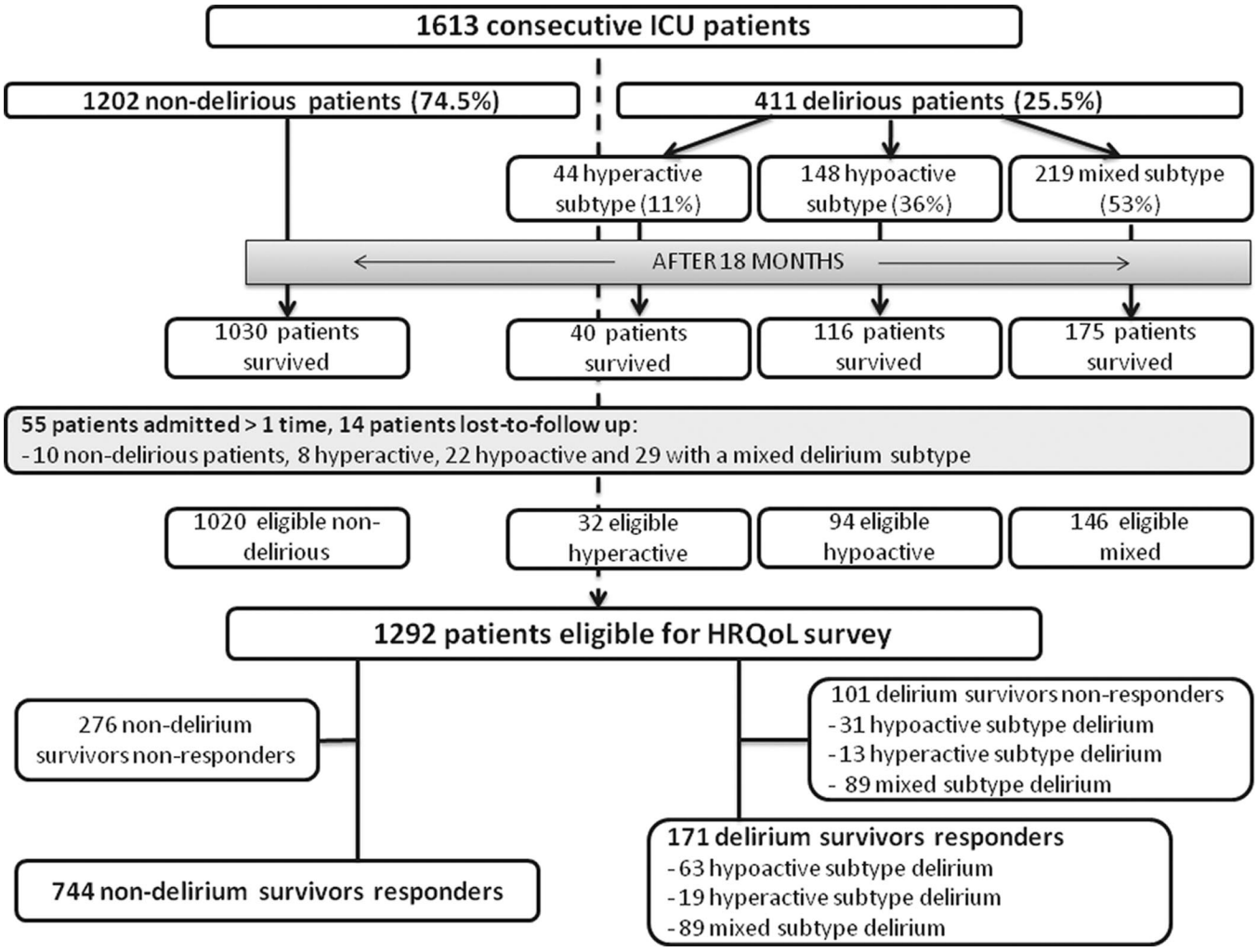

Figure 1. Flowchart of included patients for the health-related quality of life (*HRQoL*) survey. *ICU*, intensive care unit.

related characteristics of the responders and nonresponders are illustrated in Table 1. Responders with delirium during their ICU stay were significantly more likely to be admitted for urgent reasons and for sepsis, were more likely to be female than male, had a higher Acute Physiology and Chronic Health Evaluation II score, and their ICU and hospital length of stay was significantly longer compared to patients that did not develop delirium during their ICU stay (Table 2).

Differences Between Delirium and Nondelirium Patients on HRQoL

SF-36. Eighteen months (median 18, interquartile range 15–21) after ICU discharge, patients with delirium during their ICU stay rated their quality of life lower on all dimensions of the SF-36 and the physical and mental component scores compared to patients who did not

Table 1. Demographic characteristics of responders and nonresponders

Characteristics	Responders (n = 915)	Nonresponders (n = 377)	*p*
Age	65 [57–72]	60 [47–71]	<.0001
Delirium (n = 272)	171 (19%)	101 (27%)	.001
Hypoactive (n = 94)	63 (7%)	31 (8%)	
Hyperactive (n = 32)	19 (2%)	13 (3%)	
Mixed (n = 146)	89 (10%)	57 (15%)	
Gender (male)	609 (67%)	231 (61%)	.005
Sepsis (n)	28 (3%)	11 (3%)	.53
Urgent admission (n)	389 (43%)	204 (54%)	<.0001
Acute Physiology and Chronic Health Evaluation II score	14 [11–17]	13 [10–17]	.06
Length of stay-intensive care unit (days)	1 [1–2]	1 [1–3]	.03
Length of stay-hospital (days)	7 [5–14]	9 [6–18]	.001
Admission Type			<.05
Surgical	666 (73%)	225 (59%)	
Medical	131 (14%)	74 (20%)	
Trauma	41 (5%)	32 (9%)	
Neurology/neurosurgical	77 (8%)	46 (12%)	

Data are expressed as median with interquartile range unless other reported.

have delirium (Table 3). However, when adjusted for the covariates Acute Physiology and Chronic Health Evaluation II score, sepsis, ICU length of stay, gender, and urgent admission, no statistically significant differences between groups remained. The results of our ICU survivors were worse on several domains of the SF-36 compared with an age-adjusted general Dutch population (Table 3), and are in line with those of others (10).

CIS-Fatigue. Patients who suffered from delirium experienced more problems with physical exertions, expressed as a higher total CIS score, compared to the nondelirium patients (Table 3). Again, after adjusting for covariates, no significant differences in the CIS scores between the two groups remained.

CFQ. The delirium survivors reported more pronounced cognitive failure on all measured cognitive dimensions compared to patients who did not suffer from delirium. Even after adjusting for covariates, this difference between the groups persisted. Adjusted for covariates, patients who had previously had delirium tended to experience more problems with their memory ($p = .08$). Overall, their total self-reported cognitive function was significantly impaired. In addition, patients with delirium reported significantly more long-term problems with memory and concentration after ICU discharge than before when compared with nondelirium patients (Table 3).

Duration of Delirium and HRQoL

The median duration of delirium was 2 days (interquartile range 1–7, range 1–69 days). The delirium duration was significantly correlated with the dimensions memory ($r = .21$; $p = .01$) and names ($r = .18$; $p = .04$) of the CFQ. This indicates that a longer duration of delirium is related to more pronounced problems in memory and remembering names. No other statistically significant correlations between duration of delirium and the dimensions of the SF-36 and CIS-fatigue were found.

Differences in HRQoL between Subtypes of Delirium

There were no differences between the subgroups of delirium concerning age, Acute Physiology and Chronic Health Evaluation II score, gender, and sepsis. However, there were significant differences between the delirium subtypes on admission type, admission to the ICU for urgent reasons, and ICU and in-hospital length of stay (Table 4). These variables were considered as covariates. In the unadjusted database, survivors of a hypoactive delirium subtype evaluated their HRQoL on several dimensions as higher

Table 2. Demographic characteristics of responders

Characteristics	Nondelirium Patients (n = 744)	Delirium Patients (n = 171)	*p*
Age	65 [57–72]	65 [58–75]	.13
Gender (male)	508 (68%)	101 (60%)	.01
Acute Physiology and Chronic Health Evaluation II score	13 [10–16]	17 [14–20]	<.0001
Urgent admission (n)	261 (35%)	128 (75%)	<.0001
Length of stay-intensive care unit (days)	1 [1–1]	5 [2–11]	<.0001
Length of stay-hospital (days)	7 [5–11]	16 [9–37]	<.0001
Sepsis (n)	12 (2%)	16 (9%)	<.0001
Admission Type			<.01
Surgical	589 (79%)	77 (45%)	
Medical	77 (10%)	54 (32%)	
Trauma	24 (3%)	17 (10%)	
Neurology/neurosurgical	54 (7%)	23 (14%)	

Data are expressed as median with interquartile range unless other reported.

Table 3. Results of Short Form-36, checklist individual strength-fatigue, and the cognitive failure questionnaire measurements 18 months after intensive care unit discharge adjusted for covariates

Results	Nondelirium Patients (n = 744)	Delirium Patients (n = 171)	p^a	General Population Subgroup Age 55–64 yrs (22)
Short Form-36				
Physical functioning	75 [50–90]	55 [25–80]	.18	72 ± 26
Role-physical	50 [0–100]	25 [0–75]	.20	67 ± 41
Bodily pain	78 [57–100]	78 [55–100]	.26	71 ± 25
General health	60 [40–75]	55 [35–70]	.90	62 ± 20
Social functioning	88 [63–100]	75 [50–88]	.65	82 ± 23
Vitality	60 [45–75]	55 [40–75]	.94	68 ± 20
Role-emotional	100 [33–100]	100 [22–100]	.64	81 ± 35
Mental health	80 [64–92]	72 [60–88]	.26	77 ± 18
Physical component score	44 [35–52]	38 [31–48]	.66	50 ± 9
Mental component score	53 [43–58]	50 [38–57]	.61	52 ± 10
Checklist individual strength-total	28 [17–39]	32 [22–44]	.13	
Cognitive Failure Questionnaire				
Memory	7.0 [4–10]	8.0 [5–12]	.08	
Distractibility	11.0 [6–15]	11.0 [7–16]	.19	
Social blunders	6.0 [4–9]	8.0 [4–10]	.04[b]	
Names	3.0 [2–4]	3.0 [2–4]	.22	
Cognitive failure questionnaire-total	26 [17–35]	28 [19–39]	.03[b]	

Data are expressed as median with interquartile range or mean with SD (±).

[a]Adjusted for gender, urgent admission, Acute Physiology and Chronic Health Evaluation II score, sepsis, and length of intensive care unit stay using log-transformed data (not shown); [b]< .05.

Table 4. Differences between subtypes of delirium on health-related quality of life scores

Health-Related Quality of Life Scores	Hypoactive Subtype (n = 63)	Hyperactive Subtype (n = 19)	Mixed Subtype (n = 89)
Age	68 [59–75]	64 [57–75]	64 [57–75]
Gender (male)	36 (57%)	10 (53%)	55 (62%)
Acute Physiology and Chronic Health Evaluation II score	16 [14–21]	14 [13–18]	17 [15–21]
Urgent admission (N)	43 (68%)	9 (47%)	76 (85%)[a,b]
Length of stay-intensive care unit (days)	4 [2–7]	3 [1–6]	8 [3–16][a,b]
Length of stay-hospital (days)	15 [7–29]	10 [5–20]	24 [12–24][a,b]
Sepsis (n)	3 (5%)	1 (5%)	12 (14%)
Admission Type			
Surgical	29 (46%)	14 (74%)[c]	34 (38%)[a,b]
Medical	21 (33%)	3 (16%)[c]	30 (34%)[b]
Trauma	4 (6%)	2 (11%)[c]	11 (12%)
Neurology/neurosurgical	9 (14%)	0 (0%)[c]	14 (16%)[b]
Short Form-36[d]			
Physical Functioning	66 [35–85]	32 [15–71]	50 [30–75]
Role-physical	50 [0–100]	38 [0–100]	25 [0–63]
Bodily pain	78 [67–100]	57 [32–100]	78 [55–100]
General health	56 [38–70]	48 [19–65]	50 [35–65]
Social functioning	75 [63–100]	63 [34–90]	69 [50–88]
Vitality	58 [45–76]	50 [35–60]	55 [40–70]
Role-emotional	100 [33–100]	83 [17–100]	100 [0–100]
Mental health	80 [65–92][a,c]	64 [56–84]	72 [52–84]
Physical component score	37 [22–48]	41 [33–49]	36 [29–45]
Mental component score	48 [33–56]	52 [41–59]	49 [37–57]
Checklist Individual Strength[d]			
Checklist individual strength-total	30 [16–44]	33 [26–48]	33 [23–44]
Cognitive Failure Questionnaire[d]			
Memory	9 [5–12]	8 [5–13]	8 [5–12]
Distractibility	11 [7–16]	11 [6–16]	11 [7–16]
Social blunders	8 [4–9]	5 [2–11]	8 [5–11]
Names	3 [2–4]	4 [3–5]	3 [2–4]
Cognitive failure questionnaire-total	29 [20–37]	25 [17–39]	29 [19–42]

[a]Significant difference between hypoactive and mixed type subtype; [b]Significant difference between hyperactive and mixed type subtype; [c]Significant difference between hypoactive and hyperactive subtype; [d]Adjusted for urgent, length of intensive care unit and in-hospital stay, and admission type using log-transformed data (data not shown).

compared with hyperactive and mixed delirium survivors. After adjusting for the covariates, patients who had a hypoactive delirium evaluated their mental health significantly better than those who suffered from a mixed or hyperactive delirium subtype ($p = .01$ and $p = .04$, respectively).

We found no other significant differences in the SF-36, CIS-fatigue, and CFQ tests between the subtypes of delirium. Taken together, the three subgroups of delirium suffered more extensive cognitive impairment compared to the patients without delirium during their ICU stay.

DISCUSSION

We demonstrated that at median 18 months after ICU discharge there was no difference between delirium and nondelirium patients on all domains of the SF-36 and the CIS-fatigue, adjusted for relevant covariates. However, patients who suffered from delirium during their ICU stay experienced significantly more cognitive problems than those who did not, even after adjusting for covariates. Furthermore, delirium duration was significantly correlated to problems with memory and names. Interestingly, after adjusting for relevant covariates, survivors with a hyperactive or mixed subtype of delirium qualified their mental health on the SF-36 as significantly worse than the hypoactive delirium patients.

Delirium is recognized as a frequent disorder with serious short-term health-related problems and is associated with longer hospital length of stay and increased mortality rates (5, 27–30). Furthermore, in long-term studies it is recognized that hospitalized, non-ICU patients with delirium suffer from persistent cognitive impairment (31, 32). Also, ICU patients suffer from persistent cognitive impairment during long-term follow-up (7, 33, 34), but in these studies, no distinction between delirious and nondelirious patients was made. A long-term ICU study that distinguished between delirious and nondelirious patients showed that, in addition to role functioning, there was no statistically significant difference between either group (13), while in another long-term study it was observed that duration of delirium was independently associated with more pronounced cognitive impairment (6). Definite conclusions cannot be drawn from these relatively small studies because they used a more restricted HRQoL survey (13), their maximum follow-up duration was 12 months (6, 13), they mainly focused upon cognitive impairment (6), and made no adjustments for relevant covariates (13). This last point is of particular concern since more severely ill patients have a higher incidence of delirium and long-term impairments, which may not be related to each other (27).

The strength of the present study is that we used a set of validated questionnaires such as the SF-36, which is the preferred choice for the post-ICU setting (20). In addition, because of the large sample size we were able to correct for covariates, and the longer fol-

low-up emphasizes the clinical relevance of the observations.

Overall and consistently, each group of delirium subtype evaluated their cognitive functioning lower than the patients who did not suffer from delirium during their ICU stay. In our study, we found that patients who suffered from a hypoactive delirium evaluated their HRQoL on several domains of the SF-36 as less affected than the hyperactive or mixed subtype delirium patients. After adjusting for relevant covariates, the domain mental health remained significantly better in hypoactive delirium survivors. The hypoactive subtype is associated with a higher mortality rate (35, 36), a finding that we confirmed in our study, and this may have biased the results to some extent.

Our findings of prolonged cognitive impairment in ICU survivors who suffered from delirium corroborate the results of a recent meta-analysis that showed that hospitalized (non-ICU) patients with delirium have a significantly increased risk of developing dementia (37). Our results that duration of delirium correlates with prolonged cognitive problems further extends the reported effects in 77 patients 12 months after their ICU stay (6) and illustrates its clinical importance. This may indicate that interventions aimed at reducing delirium incidence and/or shortening its duration may produce long-term beneficial effects. This has not been studied yet.

We wish to acknowledge several study limitations. Firstly, it is intrinsic to long-term research in this patient group that the most severely ill may not be alive 18 months after their ICU discharge. Since the occurrence and duration of delirium is related to increased mortality (27, 29, 38), and the cognitive impairments recover in time (6), this may result in an underestimation of the effects of delirium on cognitive impairment in a long-term study such as ours. This implies that the correlation between duration of delirium and HRQoL and cognitive impairment could be underestimated in our population. Secondly, we diagnosed delirium based on minimal one positive CAM-ICU screening during patients' ICU stay. One could argue that it is better to use at least two consecutive positive CAM-ICU screenings to diagnose delirium. However, in all guidelines and delirium protocols we are aware of, patients are treated when they meet the criteria of delirium. This is the case following one positive CAM-ICU screening. According to our intensive care delirium protocol, patients are treated with haloperidol when a patient has at least one positive CAM-ICU screening. This early treatment with haloperidol may result in negative results in the following CAM-ICU's. Therefore, to include patients with two or more positive CAM-ICU scores may underestimate the presence of delirium in successfully treated patients (with haloperidol). To not recognize these patients as delirium patients is, in our opinion, not correct and not in line with daily practice. In addition, in total, only seven out of the 171 responding patients with delirium had only one positive CAM-ICU screening, and they were all treated with haloperidol following the first positive CAM-ICU. These were all patients with a hyperactive delirium subtype. The results of our study would not be influenced if these seven patients were not included. Thirdly, we adjusted for significant differences in demographic variables between nondelirium and delirium patients. Since delirium is an independent predictor of longer ICU length of stay (27), presumably independent of severity of illness, then adjustment for ICU length of stay in the analyses relating delirium to long-term outcomes may underestimate the long-term effects of delirium. Furthermore, we measured patients' long-term evaluation on HRQoL after ICU discharge once only. This can be considered as a limitation since we do not know how patients' quality of life developed during these 18 months. It appears plausible that the results would have been different if we would have also measured them in an earlier stage after discharge. Khouli et al (39) showed that a higher proportion of older patients died within 6 months after ICU discharge, and the HRQoL worsened after 6 months in the oldest group but improved in the younger group. However, taking into account the fact that cognitive impairment improved in delirium patients between 3 and 12 months after ICU discharge (6), differences between the delirium and nondelirium ICU survivors in our group was probably more pronounced earlier in the course of recovery. Since the aim of our study was to examine the long-term effects of delirium, we decided not to conduct repeated measures of the HRQoL status in a smaller group of patients, instead we chose to measure one point in time, after 18 months, in a large group of patients. This allowed adjustment for relevant covariates.

In conclusion, in this large and long-term follow-up study, we demonstrated that ICU survivors with delirium during their ICU stay had a similar adjusted HRQoL evaluation, but experienced significantly more cognitive problems in comparison to those who did not suffer from delirium. Furthermore, the duration of delirium was related to long-term cognitive problems.

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