Prevalence and Management of Delirium in Adult ICU Patients in the Netherlands: An Observational Multicenter Study

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Abstract

Background: Delirium is a common disorder in intensive care units (ICUs) and is associated with an increased length of stay in ICUs. In the past, guidelines describing interventions for prevention, assessment and treatment of delirium were published. Many studies have been performed on the prevalence and management of delirium in ICUs in other countries, but the current prevalence and management of delirium at various levels of ICUs in the Netherlands is unknown.

Aim: To determine the prevalence and management of delirium in adult ICU patients in the Netherlands, the predisposing and precipitating risk factors for delirium and variation between the ICU levels.

Method: A multicenter observational study was performed. The point-prevalence of delirium was measured on March 14th 2018. The period-prevalence was the period since admission, March 14th and the seven days thereafter. Questionnaires regarding delirium were set of in participating ICUs.

Results: In total, 26 out of 84 hospitals participated in the study. After excluding patients who were not assessed on March 14th, 383 patients were analysed. The delirium point-prevalence was 23%, and the period-prevalence 42%. Hypertension was the only predisposing risk factor that occurred more often in patients with delirium, precipitating factors were more present in patients with delirium. Regarding delirium management, protocols were present in nearly 90% of the ICUs. On March 14th, 88% of the delirium assessments was performed. Haloperidol was the most commonly used treatment for delirium. There were no patients with delirium on level 1 ICUs on March 14th and the period-prevalence was also lower.

Conclusion and recommendation: The prevalence of delirium in this study was substantial and shows the need to further improve the quality of delirium management. This can be reached by revising the guidelines and implementation of delirium management in ICUs.

Keywords: Delirium, prevalence, delirium management, ICU.

Prevalentie en management van delirium bij volwassen IC patiënten in Nederland: een observationele multicenter studie

Samenvatting

Rationale: Delirium is een veelvoorkomende aandoening op intensive care afdelingen (IC's) en wordt geassocieerd met een langere verblijfsduur op de IC. In het verleden er zijn richtlijnen met maatregelen voor preventie, assessment en behadeling van delirium gepubliceerd. Er zijn veel onderzoeken uitgevoerd naar de prevalentie en management van delirium op IC's in andere landen, maar de huidige prevalentie en management van delirium op verschillende IC levels in Nederland is onbekend.
Doel: Bepalen van de prevalentie en management van delirium bij volwassen IC patiënten in Nederland, de predisponerende en precipiterende risicofactoren voor delirium en de variatie tussen de drie IC-levels.
Methode: Er werd een observationeel multicenter onderzoek uitgevoerd. De puntprevalentie van delirium werd gemeten op 14 maart 2018. De periode-prevalentie was de periode vanaf opname op de IC, 14 maart en de zeven daaropvolgende dagen. Iedere deelnemende IC werd gevraagd vragenlijsten met betrekking tot delirium in te vullen.
Resultaten: In totaal namen 26 van de 84 ziekenhuizen deel aan het onderzoek. Na exclusie van patiënten die niet waren gescreend op 14 maart werden 383 patiënten geanalyseerd. De delirium-puntprevalentie was 23%, de periode-prevalentie 42%. Hypertensie als predisponerende risicofactor kwam vaker voor bij patiënten met een delirium, precipiterende factoren waren vaker aanwezig. Met betrekking tot delirium management waren er protocollen aanwezig in bijna 90% van de IC's. Op 14 maart werd 88% van de delirium screenings uitgevoerd. Haloperidol werd het meest gebruikt voor de behandeling van delier. Op 14 maart waren er geen delirante patiënten op level 1 IC's en ook de periode-prevalentie was lager.
Conclusie en aanbevelingen: De prevalentie van delirium in deze studie was aanzienlijk en laat de noodzaak zien om de kwaliteit van het delirium management verder te verbeteren. Dit kan worden bereikt door de richtlijn te herzien en op IC's te implementeren.

Trefwoorden: Delirium, prevalentie, delirium management, ICU.

INTRODUCTION

Delirium is a common disorder in hospitals and occurs in about 21% of admitted patients.[1,2] Delirium, also known as acute confusion is defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as a disturbance in attention and awareness, accompanied by a change in baseline cognition which cannot explained by another pre-existing, established, or evolving neurocognitive disorder. The disturbance develops over a short period of time and fluctuates during the day.[3]

Risk factors for developing delirium can be divided into predisposing and precipitating risk factors. Predisposing factors are often present long before admission and make the patient vulnerable to delirium.[4] Examples of predisposing risk factors are a history of smoking,[5–7] the use of alcohol,[5,7,13] older age,[6,8–11] pre-existing cognitive impairment[7,10,12] and hypertension.[12] Precipitating risk factors are temporary, occur during the period of admission[4] and are more modifiable than predisposing risk factors.[7] Often cited precipitating risk factors are critical illness with higher Acute Physiology and Chronic Health Evaluation (APACHE)-II or IV scores,[7,9,11,12,14–16] the use of sedatives like benzodiazepines,[10,13,14,17] and Propofol,[9] Fentanyl[9,16,17], dependence on mechanical ventilation[7–9,11,14,15], and the use of physical restraints[7,9] or other devices that preclude mobilization. Environmental factors, such as a lack of daylight and restricted visiting hours, are also considered as precipitating factors.[7,18]

Delirium can lead to deleterious effects such as a longer duration of mechanical ventilation, an increased length of stay in intensive care units (ICUs) and in hospital.[19,20]

Studies have shown the prevalence of delirium in ICUs to be between 11% and 89%.[19,20] This variation may be explained by different study design, such as the type of patients (for example only mechanically ventilated patients or patients older than 65 years) and the type of ICUs included.[19] The various Dutch studies that determined the incidence and prevalence of delirium were performed in some, predominantly university hospitals.[8,21]

University hospitals in general have more complex and specialized ICU care. The 'Central Guidance Body' (CBO) guideline of the Institute of Quality in Healthcare in the Netherlands subdivides ICUs in three levels based on size, complexity and the level of care among others.[22] These different levels may influence the prevalence of delirium, due to differences in severity of illness treated at each level. In order to establish a possible difference in delirium prevalence between these three ICU levels, predisposing and precipitating factors need to be examined. This is necessary to estimate whether differences in ICU levels are due to differences in characteristics of patients or differences in ICU characteristics.

Some precipitating risk factors of delirium may be influenced by preventive interventions. In 2010 the Dutch guideline 'delirium on the ICU'[23] and in 2013 the International 'Clinical Practice Guidelines for the management of Pain, Agitation and Delirium'[12] (PAD) in adult

patients in the ICU's were published. These guidelines provide recommendations for delirium management, which consisted of interventions for prevention, assessment and treatment of delirium. In the United States, a survey was conducted into the awareness and adoption of the 2013 PAD guidelines.[24] This survey showed that respondents who used delirium assessment tools were twice more likely to be aware of the key components of the guidelines. Dutch ICUs may differ from other countries because of differences in management and treatment of delirium but this is unknown.

No recent study has been conducted describing the prevalence of delirium in Dutch ICUs in the Netherlands and the changes in delirium management since the introduction of the PAD guidelines. If current practice regarding delirium and its shortcomings are known, improvements can be made. Therefore, the main objective of the present study was to determine the variation in delirium prevalence rates in adult patients in a number of Dutch ICUs. Secondary objectives were exploring the predisposing and precipitating risk factors for delirium, exploring variation between ICUs in delirium management regarding prevention, assessment and treatment and determining variation in delirium prevalence rates and delirium management among the three ICU levels.

METHOD

Study design, setting and population

This study was conducted as an observational multicenter study. This design makes it possible to gain insights into the actual prevalence of delirium and how ICUs handle delirium management. A one-day point-prevalence of delirium was taken on March 14th and a period-prevalence was taken of the period since admission, March 14th and the seven days thereafter. The strengthening the reporting of observational studies in epidemiology (STROBE) statement checklist was used to make sure all important elements were taken into account in this report.[25]

The study population existed of ICU patients and the ICU staff. Patients were eligible if they were 18 years of age or older and stayed in or were admitted to the ICU on day one of the study period of seven days. Patients were excluded when no delirium assessment was performed on March 14th. In every participating ICU one physician or (research) nurse was asked to complete a questionnaire with departmental data to provide insight into the process of delirium management. All types of ICUs could participate for example medical, neurological or cardiac-surgical ICUs. When ICUs consisted of different locations with different levels, a department questionnaire was entered per location.

Sample size calculation

This study had an exploratory character for which a power calculation was redundant. To estimate the number of patients that could be included, previous ICU admission data were used. Based on 2016 data of the National Intensive Care Evaluation (NICE) where there was a 73% occupancy rate of 1210 beds,[26] an assumption was made that approximately 883 patients would present in Dutch ICUs on any given day and may be eligible for inclusion in this study. Assuming that over a quarter[27] of all ICUs would participated in the study, a sample size of 238 patients was expected.

Data collection

The primary objective point-prevalence rate of delirium was measured on World Delirium Day, March 14th 2018. A patient was considered to have had delirium if there were one or more positive delirium assessments on March 14th. In addition, it was asked whether the patient had been delirious before March 14th and the seven days thereafter.

Primary outcome measure; delirium screening

Delirium prevalence was measured with the local standard of care scales used by ICUs. For the assessment of delirium, the Confusion Assessment Method, adapted for the use in the ICU (CAM-ICU), and the Intensive Care Delirium Screening Checklist (ICDSC) are the most common tools and recommended by the international guideline.[12] Both tools are validated relative to the golden standard, which are the DSM criteria used by a specialized psychiatrist.[28,29] In a systematic review of the CAM-ICU versus the ICDSC, sensitivity was 80% vs. 74% and specificity was 95.9% vs. 81.9%.[30]

The scores of the Richmond Agitation Sedation Tool (RASS) or other scales used by hospitals were registered. Patients with a RASS of -4 and -5 were not screened for delirium.[31,32]

Secondary outcome measures; risk factors, delirium management and ICU levels

Other outcome measures were the precipitating and predisposing risk factors, delirium management and the differences between the three ICU levels. For the preparations of the questionnaires, the Dutch delirium guideline[23] and international PAD guideline were used.[12]

Some of the precipitating risk factors are also preventive parameters. For example, the administration of benzodiazepines and deeper sedation increases the risk of delirium.[12] Daily sedation interruptions are intended to prevent deep sedation. Other risk factors such as severity of illness, measured by the sepsis-related organ failure assessment (SOFA) score and the APACHE II and/or IV, mechanical ventilation, renal replacement therapy (RRT), and use of vasopressors were scored. Possible predisposing risk factors scored were age,

comorbidities, pre-existing cognitive impairment, hypertension and a history of alcohol use and/or smoking.

Delirium management consists of three aspects: prevention, assessment and treatment of delirium. Preventive interventions were divided into non-pharmacological and pharmacological interventions. Among non-pharmacological measures for prevention of delirium, for example early mobilization and promoting sleep were recommended. Environmental factors like a clock and daylight in the patient room and the presence of family were also explored. Pharmacological measures include the avoidance of the use of benzodiazepines for sedation.[12] Propofol and dexmedetomidine are preferred for sedation.[12] Furthermore, it is recommended to start analgesia before sedation.[12] Therefore, if patients were sedated, analgesics should also be used. Besides the delirium and sedation score, the study asked whether a pain score was performed. Data on the treatment of delirium were collected per patient.

Each participating ICU was asked at which level (1, 2 or 3) it operated and if protocols and procedures were implemented for delirium management.

Statistical analysis

All data are quantitative and are presented by descriptive statistics with frequencies and percentages for categorical variables and means with standard deviations for continuous variables or median and interquartile range [IQR] depending on the distribution. Statistical analyses were performed using IBM SPSS Statistics version 24 (Amork, New York USA).

The presence of delirium and the subtypes of delirium were nominal variables, which were presented descriptively. The precipitating and predisposing risk factors for the period-prevalence of delirium variables were tested with the Students t-test for continual variables with a normal distribution and the Mann-Witney-U test for variables with a skewed distribution. Categorical variables were tested with the Chi-square test or Fisher's exact test depending on the number of events per group.[33] A continuity correction was performed for 2x2 tables. For tables larger than 2x2, when the overall Chi Square was significant, a post-hoc test with the adjusted residuals was performed.[34] Because this is an exploratory study, no post hoc for multiple comparisons like the Bonferroni was performed. Variables regarding delirium management were also presented descriptively. For the variation in delirium period-prevalence rates and delirium management between the three ICU levels the Chi Square was applied as described before. Univariate analyses for continual variables were performed with the ANOVA (normal distribution) or Kruskal-Wallis test (skewed distribution). The null hypothesis stated that there is no association between the risk factors and different ICU levels and the presence of delirium. A p value of $<.05$ means there is a relationship between the two variables.

Study procedures

On February 8th 2018 ICUs in the Netherlands were approached at the congress of Dutch intensive care physicians organized by the Dutch association for Intensive Care (NVIC). Furthermore, the networks of EB, EW and MB were contacted by email to participate in this study. All patients admitted to the ICU on March 14th were entered into the case report form (CRF) by the participating hospitals. Patients who were admitted to or discharged from ICUs on March 14th could also be included. Each participating hospital performed delirium assessment and management as usual. Because not all hospitals structurally performed delirium scores, they were stimulated to screen for delirium. To gain insight in the compliance with the delirium score, the score rate on a normal day was also reported.

Ethical issues

This study was conducted according to the principles of the Declaration of Helsinki.[35] The Medical Ethical Committee of the Radboud Universal Medical Centre (UMC) approved the study (study number 2018-4088). Since this was an observational, non-interventional study the study was exempted from the Medical Research Involving Human Subjects Act (WMO).[36] Therefore, informed consent was not requested, patients were only informed about the study. As patients data were used the rules of the Dutch Data Protection Act and the Medical Treatment Agreement Act (Wbp)[37] were followed. Hospital and patient data were entered by the participating hospitals in a validated data management system (CastorEDC) with pseudo-anonymized codes. A patient identification list was safeguarded by the various participating hospitals. Data are stored for up for fifteen years after completion of the study in the Digital Research Environment of the RadboudUMC.[38]

RESULTS

In total, 26 (31%) out of 84 Dutch hospitals participated in the study. Two hospitals have multiple locations with different ICU levels therefore 28 ICU were analysed. On March 14th 403 (88%) out of 458 beds were available. In total 410 patients of 18 and older were entered into the e-CRF of which 27 patients were excluded because they were not assessed for delirium on March 14th. The mean age of the patients included was 64 years old and 233 (61%) of the patients were male. Other patient characteristics are shown in Table 1.

Prevalence

Figure 1 shows a flowchart of the study patients. 296 (77%) of the remaining 383 patients were screened for delirium on March 14th and 87 (23%) patients were not assessable. The most common reason why patients could not be screened was a comatose state (RASS -3/-

5). The point-prevalence on March 14th was 23% and the period-prevalence of the period since admission, March 14th and the seven days thereafter was 42%.

Figure 1

Predisposing and precipitating factors for the period-prevalence

Predisposing factors evaluated that differed significantly between patients with a delirium and without a delirium, was hypertension, but not age and gender. Alcohol use and smoking data were not reliable because of the large number missing values (51 vs. 59 missing values respectively). These data were not available in the relevant medical or nursing anamneses. All the precipitating factors evaluated differed significantly between delirious and non-delirious patients. Delirious patients had higher APACHE scores and more often an infection. Other predisposing and precipitating factors are shown in Table 1.

Table 1

Delirium management

Nearly all ICUs (89%) worked according to a PAD protocol and 23 ICUs (82%) had a PAD team. ICU characteristics are shown in Table 2.

Non-pharmacologic preventive interventions like mobilization were applied in 68% of the patients, of which 26% was mobilized in bed. A physiotherapist was consulted for 75% of the patients. Of the delirious patients, 41% were immobilized through fixation on March 14th and 11% of the non-delirious patients. Environment factors like interior of the patient room were implemented in most of the ICUs. Only 6 (21%) ICUs use continuous visiting hours.

Pharmacologic preventive interventions, like the use of dexmedetomidine were administered to 22 patients on March 14th. Of the sedated patients, in 46% the sedation was interrupted. Other preventive interventions are shown in Table 2.

Most hospitals used the CAM-ICU to screen for delirium, two hospitals used the ICDSC, one hospital used the DOS (Delirium observation screening) – but will shortly move to the CAM-ICU – and one hospital use the RASS in combination with clinical view. All hospitals used the RASS to screen sedation and agitation. On March 14th, 88% of the delirium assessments were performed in arousal patients. The mean compliance with delirium assessment on a regular day was 69%.

For the treatment of delirium according to the protocol, haloperidol was the first-choice medication in 26 (93%) of the ICUs. On March 14th, 143 (37%) of the patients stayed in one of the participating ICU were given intravenous sedatives, 191 (50%) received

intravenous pain control, and 82 (20%) patients received medication for the treatment of delirium.

Table 2

ICU levels

Seven level 1, eight level 2 and twelve level 3 ICUs participated in this study (Table 2). On March 14th 37 (10%) patients were admitted to a level 1 ICU, 90 (23%) patients to a level 2 ICU and 256 (67%) patients to a level 3 ICU.

Prevalence of delirium

The point prevalence of delirium on March 14th was 20% on the level 3 and level 2 ICUs, and there were no delirious patients on ICUs of level 1 ($P < 0.01$). For the period-prevalence level 1 ICU showed also a lower delirium prevalence rate as compared to the other level of ICUs (Table 3).

Predisposing and precipitating risk factors

Regarding predisposing risk factors patients on level 2 ICUs were older and patients on level 1 ICUs had more comorbidities (Table 3). Of the precipitating risk factors APACHE scores differs not significantly. The higher the level the more often patients were mechanically ventilated ($P < 0.001$).

Delirium management

Level 2 and 3 ICUs more often worked with a PAD team and protocol as compared with level 1 ICUs. The compliance with delirium assessment on a regular day was the lowest on level 1 ICUs (Table 3).

Table 3

DISCUSSION

In this multicentre study, in which nearly a third of the Dutch hospitals participated the delirium point-prevalence on March 14th was almost a quarter and the period-prevalence about 40%. Hypertension was the only predisposing risk factor that occurring more often in patients with delirium. All precipitating factors were more present in patients with delirium. Delirium management protocols were applied in almost all of the participating level 2 and 3 ICUs. A PAD team was present in almost 90% of the ICUs. Concerning delirium prevention,

only 21% of the ICUs have continuous visiting times. For the assessment of delirium the CAM-ICU is the most frequently used screening tool. On March 14th, 88% of the delirium assessments were performed in arousal patients. Patients with a RASS -3 were reported as not assessable. Haloperidol was first choice for pharmacological treatment in most ICUs and most frequently used for the treatment of delirium. On March 14th there were no patients with delirium on level 1 ICUs and the period-prevalence was also significantly low.

The point-prevalence of 23% in this study is lower as compared to a delirium prevalence of 32% in a point-prevalence study conducted in America and Spain.[13] This may be explained by the inclusion of patients in the present study with a length of stay on ICU less than 24 hours. The period-prevalence of 42% in this study was higher than in a systematic review, which included 42 studies with different inclusion criteria.[20] This is remarkable because most of these studies used inclusion criteria like mechanical ventilation, admission > 24 hours, and age over 65 years. In this study these inclusion criteria were not apply, and therefor a lower prevalence was expected. In addition, patients in the present study had a higher APACHE II score than in the systematic review.

The only significant predisposing risk factor that emerged from this study, hypertension is also mentioned as a risk factor in the international PAD guideline,[12] but this is based on only two studies. No recent study has analysed hypertension as a risk factor for delirium. One of the important precipitating risk factors, a high severity of illness at admission, measured with the APACHE score, is mentioned in both guidelines and was also significant in this study. Other precipitating risk factors such as mechanical ventilation were also significant but are related with the severity of illness.

Regarding delirium management, in this study most of the environmental factors that may prevent delirium were managed in this study. However, visiting hours were restricted in most of the ICUs. Flexible visiting times have the potential to reduce delirium.[18] Delirium assessment was noticed as not assessable for patients with RASS -3. The CAM-ICU manual suggest that delirium assessment is possible if the patients RASS is ≥ -3.[39] In this study 89% of the ICUs used a delirium protocol, in contrast to an American survey in 2014 where only 46% of the respondents worked in an ICU where delirium protocols were implemented.[24] In the same survey haloperidol (78%), second-generation antipsychotics (75%) and dexmedetomidine (37%) were the most prescribed pharmacologic agents to treat delirium. In accordance with the Dutch guideline, in the current study haloperidol was the first agent of choice to treat delirium in 93% of the ICUs. Second choice agents were second-generation antipsychotics (54%) and dexmedetomidine (46%). The international PAD guidelines do not recommend haloperidol for the treatment of delirium in contrast to the Dutch guideline.

Surprisingly, no patients with a delirium were present on level 1 ICUs. The reason is unclear. No differences in APACHE score and number of patients on mechanical ventilation

were observed between ICUs although these precipitating factors affect the chance to develop a delirium.

Strength of the current study is that it gives an impression of the care with regard to delirium and delirium management as it is applied at the moment. Another strength is the sample size, since it included almost one third of all hospitals in the Netherlands. This response rate was higher than expected. Furthermore, all the ICU levels were represented, so the study gathered information about all types of ICU, not only university hospitals and ICUs with higher levels of care.

This study has several limitations. First, the ICUs performed assessment of delirium as usual. Some hospitals that do not regularly screen for delirium did so on March 14th, and stimulated assessments to provide a score. Nevertheless there were still many missing delirium scores. On the other hand, this study shows that delirium assessments are not always performed regularly. Second, the period-prevalence had a retrospective character; this limits the reliability of the prevalence rate. Because not all hospitals regularly assess delirium, the rate could be an underestimation of the actual rate. Third, the point-prevalence was on March 14th, this was just at the end of the influenza epidemic, so this can give a seasonal effect. Finally, nearly all hospitals used a PAD protocol. Except for the first- and second-choice delirium medication, the study did not asked which medication for pain and sedation were included in the protocols. Only the use of medication on March 14th was recorded. Thus it remains unclear to which extent hospitals follow the guidelines in this aspect.

This study gives the first prevalence rates of delirium in a large number of various type of ICUs in the Netherlands. This study is the first on delirium management in the Netherlands and thus may prove a starting point to improve delirium management and subsequent improvement of quality of care. The questions used in this study were mainly based on the international PAD guideline because the Netherlands does not have one PAD guideline but two separated guidelines; one for delirium[23] and one for pain and sedation.[23] These two guidelines contradict each other sometimes for example on the use of benzodiazepines for long-term sedation. The international PAD guideline recommended an integrated pain, agitation and delirium protocol. Therefore, it is advised to develop an integrated Dutch PAD guideline for implementation in ICUs in the Netherlands. After the implementation, a new study on delirium prevalence and delirium management should be performed in order to compare the prevalence rates and compliance to the new guideline.

In conclusion, a substantial number of ICU patients admitted on March 14th, delirium is present or at another time during their admission. Hypertension was the only predisposing risk factor that occurred more often in patients with delirium. All precipitating factors were significantly more present in patients with delirium. On March 14th there were no delirious

patients on level 1 ICUs and the period-prevalence was also significantly lower at this level of ICU, although protocols were implemented less frequently in this type of ICU.

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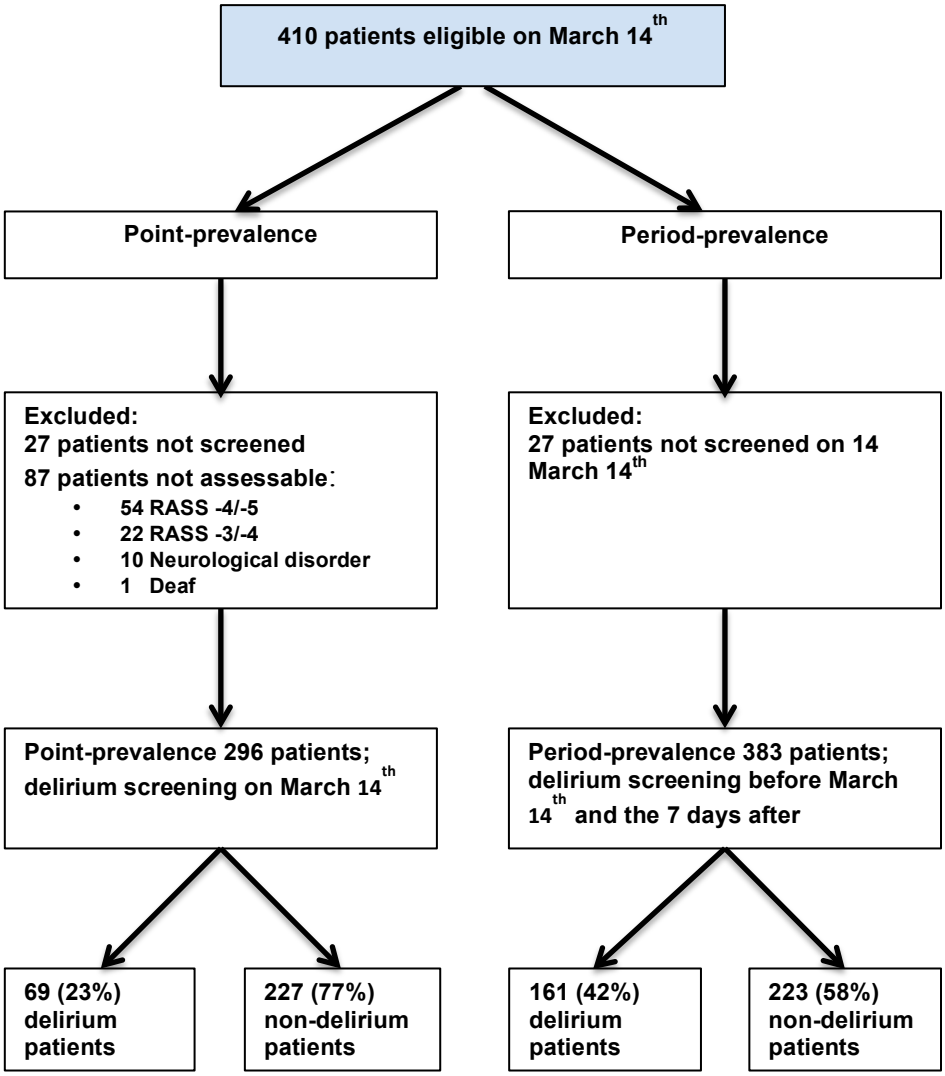

Fig. 1 Flowchart of study patients

Table 1 Patient characteristics of delirium and non-delirium patients; period prevalence

Variables	**All patients** *N = 383*	**Delirium patients** *N = 161 (42%)*	**Non-delirium patients** *N = 222 (58%)*	***P*-value**
Predisposing factors				
Age in years, mean (SD)	64 (14)	65 (13)	63 (14)	0.1
Male, *N* (%)	233 (61)	103 (64)	130 (59)	0.33
Comorbidities, *N* (%)	91 (24)	35 (22)	56 (25)	0.43
• Diabetes	77 (20)	38 (24)	39 (18)	0.18
• Diabetes complications	14 (4)	8 (5)	6 (3)	0.37
• Liver disease	10 (3)	5 (3)	5 (2)	0.75
• Severe liver disease	1 (0.3)	0 (0)	1	0.42
• Malignity	52 (14)	16 (10)	36 (16)	0.11
• Metastases	11 (3)	2 (1)	9 (4)	0.13
• AIDS	1 (0.3)	1 (1)	0 (0)	0.42
• Severe kidney disease	45 (12)	25 (16)	20 (9)	0.07
• Heart failure	51 (13)	24 (15)	27 (12)	0.52
• Myocardial infarction	44 (11)	23 (14)	21 (9)	0.19
• COPD	84 (22)	35 (22)	49 (22)	1.00
• Peripheral vascular disease	36 (10)	14 (10)	22 (9)	0.88
• CVA or TIA	41 (11)	23 (14)	18 (8)	0.08
• Dementia	0 (0)	0 (0)	0 (0)	
• Hemiplegia	1 (0.3)	1 (1)	0 (0)	0.42
• Connective tissue disease	2 (0.5)	0 (0)	2 (1)	0.51
• Stomach ulcer	3 (1)	3	0 (0)	0.07
• Preexistence cognitive disorder	9 (2)	2 (1)	7 (3)	0.31
• Other	77 (20)			
Hypertension, *N* (%)	156 (41)	76 (48)	80 (36)	0.04
Alcohol use, *N* (%)	101 (26)	49 (37)	51 (26)	0.05
> 14 EH/week, *N* (%)	19 (3)			
Active smoking, *N* (%)	112 (29)	57 (42)	55 (28)	0.02
Precipitating factors				
Type of admission, *N* (%)				
• Medical	226 (59)	112 (70)	114 (51)	<0.01
• Surgical	76 (20)	22 (14)	54 (24)	<0.01
• Cardiac surgical	38 (10)	13 (8)	25 (11)	0.32
• Trauma	13 (3)	5 (3)	8 (4)	0.76
• Neurological	17 (5)	12 (5)	5 (3)	0.27
• Neurosurgical	13 (3)	4 (3)	9 (4)	0.42
Infection, *N* (%)	173 (45)	91 (57)	82 (37)	<0.0001
• SIRS	31 (8)	13 (42)	18 (58)	
• Sepsis	73 (19)	38 (53)	34 (47)	
• Severe sepsis	22 (6)	13 (59)	9 (41)	
• Septic shock	45 (12)	27 (61)	17 (39)	
APACHE II points, mean (SD)	19 (9)	21 (8)	17 (9)	<0.01
APACHE IV points, mean (SD	67 (31)	74 (30)	63 (30)	<0.01
Ventilation during admission, *N* (%)	305 (79)	149 (93)	156 (70)	<0.01
Vasopressor first 24h, *N* (%)	250 (65)	120 (75)	130 (58)	<0.01

Table 2 Department characteristics at the different levels

Variables	Level 1	Level 2	Level 3	All
Number of hospitals, *N (%)*	7	8	13	28
Number of beds, *N* (%)	85	102	271	458
Number of available beds on 14 March, *N* (%)	71 (81)	93 (91)	239 (88)	403 (88)
Type of department, *N* (%)				
• Medical	7 (100)	8 (100)	13 (100)	28 (100)
• Surgical	7 (100)	8 (100)	13 (100)	28 (100)
• Cardiac-surgical	0 (0)	0 (0)	6 (46)	6 (21)
• Trauma	3 (43)	3 (38)	10 (77)	16 (57)
• Neurosurgical	1 (14)	1 (13)	8 (62)	10 (36)
• Neurology	6 (86)	4 (50)	10 (77)	20 (72)
PAD protocol, *N* (%)	5 (71)	8 (100)	12 (92)	25 (89)
PAD team, *N* (%)	4 (57)	8 (100)	11 (85)	23 (82)
Delirium screening				
• CAM-ICU, *N* (%)	6 (75)	6 (75)	12 (100)	24 (86)
• ICDSC, *N* (%)	0 (0)	2 (25)	0 (0)	2 (7)
• Other, *N* (%)	2 (25)	0 (0)	0 (0)	2 (7)
Compliance delirium assessment on a regular day	50 [25-80]	88 [73-95]	90 [50-98]	80 [50-94]
Sedation/agitation scale; RASS, *N* (%)	7 (100)	8 (100)	13 (100)	28 (100)
Pain scale, *N* (%)				
• NRS (for conscious patients)	7 (100)	7 (88)	12 (92)	26 (93)
• CPOT	3 (43)	6 (75)	7 (54)	16 (57)
• BPS	0 (0)	2 (25)	3 (23)	5 (18)
• Other (VAS)	0 (0)	1 (13)	1 (8)	2 (7)
Early mobilization, *N* (%)	7 (100)	8 (100)	13 (100)	28 (100)
• < 24h	6 (86)	7 (88)	7 (54)	20 (71)
• < 48h	0 (0)	1 (13)	4 (31)	5 (18)
• < 72h	1 (14)	0 (0)	2 (15)	3 (11)
What is meant by early mobilization? *N* (%)				
• Mobilization in bed, passive	6 (86)	7 (88)	11 (85)	24 (86)
• Mobilization in bed, sitting	5 (71)	8 (100)	12 (92)	25 (90)
• Cycling in bed	4 (57)	5 (63)	9 (69)	18 (64)
• Passive transfer bed-chair	3 (43)	6 (75)	10 (77)	19 (68)
• Sitting at bedside	5 (71)	6 (75)	10 (77)	21 (75)
• Active transfer bed-chair	6 (86)	5 (63)	8 (62)	19 (68)
• Walking	1 (14)	3 (38)	5 (39)	9 (32)
Sedation interruption for mobilization, *N* (%)	3 (43)	2 (25)	4 (31)	9 (32)
Which patients were never mobilized early, *N* (%)				
• Intubated patients	0 (0)	0 (0)	0 (0)	0 (0)
• RRT	5 (71)	1 (13)	2 (15)	8 (29)
• ECMO/IABP	1 (14)	4 (50)	12 (92)	17 (61)
• Inotropes	6 (86)	4 (50)	7 (54)	17 (61)
• PEEP > 10cm H_2O / FiO_2 > 60mmHg	2 (29)	3 (38)	4 (31)	9 (32)
• RASS -4/-5 or 3/4	1 (14)	2 (25)	7 (54)	10 (36)
• Catheter in Femoralis	0 (0)	0 (0)	2 (15)	2 (7)
After 10 pm doctors visit the patient, *N* (%)				
• Yes, by default	0 (0)	4 (50)	7 (54)	11 (39)
• Yes, on indication	7 (100)	4 (50)	5 (39)	16 (57)
• No, never	0 (0)	0 (0)	1 (8)	1 (4)
Environment preventive interventions, *N* (%)				
• Earplugs	4 (57)	7 (88)	8 (62)	19 (68)
• Reduce light	7 (100)	8 (100)	13 (100)	28 (100)
• Clock	7 (100)	8 (100)	13 (100)	28 (100)
• Whiteboard	3 (43)	3 (38)	8 (62)	14 (50)
• Television	7 (100)	7 (88)	12 (92)	26 (93)
• Space for personal items	6 (86)	8 (100)	12 (92)	26 (93)
• Visit				
• Continuous visit	0 (0)	2 (25)	4 (31)	6 (21)
• Set visiting times > 5 hours a day	3 (43)	4 (50)	3 (23)	10 (36)
• Set visiting times < 5 hours a day	4 (57)	2 (25)	6 (46)	12 (43)
First choice of drug treatment for delirium, *N* (%)				
• Haloperidol	7 (100)	8 (100)	11 (85)	26 (93)
• Dexmedetomidine/clonidine	0 (0)	0 (0)	1 (8)	1 (4)

Variables	Level 1	Level 2	Level 3	All
Second choice of drug treatment for delirium, *N* (%)				
• Haloperidol	0 (0)	0 (0)	0 (0)	0 (0)
• Olanzapine	1 (14)	3 (38)	0 (0)	4 (14)
• Dexmedetomidine/clonidine	2 (29)	5 (63)	6 (46)	13 (46)
• Quetiapine	2 (29)	3 (38)	6 (46)	10 (36)
• Benzodiazepine	1 (14)	0 (0)	1 (8)	2 (7)
• Clozapine	0 (0)	0 (0)	1 (8)	1 (4)
Treatment, *N* (%)				
• All patients with delirium	3 (43)	6 (75)	6 (46)	15 (54)
• Symptomatic	3 (43)	2 (25)	3 (23)	8 (29)
• Hypoactive delirium variably	1 (13)	0 (0)	2 (15)	3 (11)
• Causal			1 (8)	
Is analgesics start before sedation, *N* (%)				
• Yes, by default	2 (29)	2 (25)	4 (31)	8 (29)
• Yes, on indication	3 (43)	1 (13)	6 (46)	10 (36)
• Yes, always in combination	2 (29)	5 (63)	2 (15)	9 (32)

Table 3 Patient characteristic and the different levels

Variable	***Level 1*** N = *37*	***Level 2*** N = *90*	***Level 3*** N = *256*	**P-*value***
Delirium period-prevalence, *N* (%)	5 (13)	40 (44)	116 (45)	<0.001[a]
Delirium March 14th, *N* (%)	0	18 (20)	51 (20)	<0.001[a]
Non-delirium March 14th, *N* (%)	29 (76)	55 (61)	143 (56)	
Not assessable March 14th, *N* (%)	9 (24)	17 (19)	62 (24)	
Predisposing factors				
Age in years, mean (SD)	62 (14)	67 (14)	63 (13)	0.04
Gender Male, *N* (%)	18 (47)	44 (49)	172 (6)	<0.001[c]
Comorbidities, *N* (%)	15 (40)	13 (14)	64 ((25)	<0.01
Hypertension, *N* (%)	13 (34)	37 (42)	107 (42)	0.65
Precipitating factors				
LOS hospital, median [IQR]	3 [2-14]	6 [2-18]	7 [2-17]	0.26
LOS ICU, median [IQR]	3 [1-10]	4 [2-11]	3 [1-14]	0.42
Type of admission, *N* (%)				
• Medical	18 (47)	69 (77)	139 (54)	<0.0001[b]
• Surgical	19 (50)	19 (21)	39 (15)	<0.0001[a]
• Cardiac-surgical	0	0	38 (15)	<0.0001[c]
• Trauma	0	1 (1)	12 (5)	
• Neurological	1	1 (1)	15 (6)	
• Neuro-surgical	0	0	13 (5)	
Infection, *N* (%)	17 (45)	50 (56)	106 (41)	0.07
APACHE II points, med [IQR]	17 [13-23]	18 [11-26]	19 [13-25]	0.89
APACHE IV points, med [IQR]	58 [44-77]	69 [35-98]	70 [49-91]	0.14
SOFA score march 14th, med [IQR]	3 [1-5]	4 [2-9]	6 [3-10]	<0.001
Ventilation March 14th, *N* (%)	17 (45)	46 (51)	164 (64)	<0.006[c]
• Invasive	13 (34)	42 (47)	147 (57)	
• NIV/optiflow	4 (11)+	4 (4)	17 (7)	
Ventilated before and March 14th, *N* (%)	22 (58)	64 (72)	219 (86)	<0.0001[c]
Ventilation days, med [IQR]	4 [2-11]	8 [3-18]	5 [1-15]	0.44
Vasopressors 1e 24h, *N* (%)	20 (53)	55 (61)	175 (68)	0.11
RRT, *N* (%)	1 (3)	9 (10)	31 (12)	0.21
Second admission, *N* (%)	1 (3)	7 (8)	23 (9)	
Sedatives, *N* (%)	11 (29)	32 (36)	100 (39)	0.45
Benzodiazepines, *N* (%)	4 (11)	8 (9)	29 (11)	0.81
Propofol, *N* (%)	6 (16)	17 (19)	73 (29)	0.07
Dexmedetomidine / Clonidine, *N* (%)	2 (5)+	9 10)	24 (9)	
Analgesics intravenously, *N* (%)	26 (68)	32 (36)	133 (52)	<0.01[b]
Opioids, *N* (%)	9 (24)	31 (34)	172 (33)	0.47
Medication to treat delirium, *N* (%)	1 (3)	25 (28)	56 (22)	<0.01[a]
Haloperidol, *N* (%)	1 (3)	21 (23)	45 (18)	0.02
Dexmedetomidine / Clonidine, *N* (%)	0	6 (7)	13 (5)	
Environment				
Physical restraints, *N* (%)	5 (13)	19 (22)	50 (20)	0.523
Daylight	36 (97)	78 (87)	250 (98)	
Patient room				
• Single room	29 (78)	74 (82)	173 (68)	
• Double room	0 (0)	5 (6)	48 (19)	
• > 2	8 (22)	11 (12)	35 (13)	

[a] Significantly at level 1
[b] Significantly at level 2
[c] Significantly at level 3