

ICU delirium: what is different between the type of diseases?

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Research

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Abstract

Background: Delirium is an acute neurological disorder that is quite common complication in intensive care unit (ICU) patients. However, there are no studies to focus on risk factors vary from disease to disease. The purpose of our study was to identify the risk factors and prognosis of delirium in patients with different disease types.

Method: We conducted an observed study of consecutive patients from September to November 2016, who underwent surgical operation or with poor conservative treatment were admitted to the ICU. The patients were screened for delirium by using the diagnostic tools of Richmond Agitation Sedation Scale (RASS score) and the Confusion Assessment Method ICU (CAM-ICU).

Results: A total of 406 patients met the inclusion criteria in our study. The overall incidence of ICU delirium was 45.8% (186/406), the delirium was highest in patients with brain disease (68%), followed by pulmonary disease (63%) and sepsis/shock (49%). The risk factors are different for different types of disease, for heart and vascular disease subgroup, only sleep quality (OR=0.236, $p=0.001$) was independent risk factor for delirium. For abdominal disease subgroup, age (OR=2.514, $p=0.002$), vasoactive drugs (OR=13.799, $p=0.002$), and sleep quality (OR=0.114, $p=0.001$) were risk factors for the delirium. And for sepsis and septic shock subgroup, age (OR=1.100, $p=0.022$), APACHE II scores (OR=1.255, $p=0.001$) and sleep quality (OR=0.090, $p=0.034$) were risk factors for the delirium. ICU delirium is associated with worse outcomes including ICU stays ($P<0.001$) and 28-day mortality ($P=0.001$). The difference of ICU stays between delirium and non-delirium groups in the subgroup of heart and vascular disease ($P<0.001$), pulmonary disease ($P=0.011$), sepsis/septic shock ($P<0.001$) and cerebral disease ($P=0.011$) were consistent with the general population. But subgroup of sepsis/septic shock was the only one whom has the significant difference in the 28-day mortality ($P=0.006$) between delirium and non-delirium groups.

Conclusion: The incidence and risk factors of delirium varied greatly with the type of disease. Age and sleep quality were independent risk factors for the development of delirium in most subgroup diseases. The prognosis of delirium was different in different disease types, among them, patients with sepsis/septic shock associated delirium have the worst prognosis.

Background:

Delirium is an acute neurological disorder that is frequently observed in Intensive Care Unit (ICU) patients with an incidence ranging from 11–80% [1,2,3]. It is characterized by transitory changes of consciousness and cognition, generally for a short period of time [4]. Patients that developed this disorder performed worst in the clinical outcomes, contributing to extended length of ICU stay, higher mortality rate, neurological sequelae such as cognitive impairment and significant risk of death after six months which represents a significant burden for patients and relatives, as well as to the health care system [5,6,7].

Considering the negative aspects of delirium on patients' prognosis, the early recognition and amelioration of modifiable risk factors and treatment of underlying conditions that predisposes the individual to delirium by health professionals is important in ICU [8]. Yamaguchi et al [9] showed that older age and biopsychosocial vulnerability assessed by the COMPRI were risk factors of ICU delirium. ICU delirium was a predictor of increased mortality and associated with prolonged ICU and hospital LOS. ICU delirium was an independent risk factor for having social worker's consultation after ICU discharge. Tse L et al's [10] retrospective cohort study founded that patients undergoing cardiopulmonary bypass grafts (CABG) with age ≥ 64 years, history of delirium, history of stroke/transient ischemic attack, cognitive impairment, depression, and preoperative use of beta-blocker(s) were

associated independently with delirium. And Wang et al[11] suggested advanced age (> 70 years), the use of general anesthesia, longer surgical duration (> 3 hours), the presence of intraoperative hypercapnia and hypotension, the presence of preoperative affective dysfunction, and the presence of postoperative sleep disorders appear to be associated with the development of postoperative delirium in geriatric patients after orthopedic surgery. The incidence of delirium varied greatly with the type of disease, so it is important to further understand the risk factors for delirium in different diseases.

Currently, the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) [9] and the Intensive Care Delirium Screening Checklist (ICDSC) [13] are the most valid and reliable tools for monitoring delirium in adult ICU patients since the 2013 American College of Critical Care Medicine (ACCM)/Society of Critical Care Medicine (SCCM) clinical practice guidelines for pain, agitation, and delirium (PAD) have recommend [14]. CAM-ICU has shown good validity for identifying delirium in critically ill patients [15].

This study was used the Confusion Assessment Method for the ICU (CAM-ICU) to evaluated the delirium. Our main purpose was to evaluate the incidence and prognosis of delirium and illustrate those specific characteristics that lead to delirium in ICU. We also focused on this particular subject in patients with different disease types to find out their risk factors which would predispose patients to delirium and evaluated the prognosis of patients with different diseases respectively, to provides clinical basis for early identification and prognosis of delirium in ICU patients.

Methods

Study design

This prospective observational study was conducted in a mixed medical 33-bed adult general ICU in a 3500-bed hospital in Changsha, China. The ICU was a closed unit with an accredited intensivist responsible for the management of all patients. Ward rounds were conducted by the intensivist twice a day when treatment goals/plans were reviewed. The main practices associated with sleep promotion during the time in which the study was conducted was dimming the main lights at night.

Patients population

Patients were included if aged > 18 years and likely to be treated in ICU for > 24 hours and able to give informed consent on their own behalf. Patients provided informed consent with written confirmation by their next of kin in cases where the patient was unable to sign the consent form.

Exclusion criteria included a history of sleep disorders, psychiatric illness requiring medication, history of psychological problems, pre-existing cognitive problems, a known diagnosis of dementia or central neurological impairment confirmed by radiological scan. Patients with a Richmond Agitation and Sedation Scale 4 or more during their entire ICU stay were excluded, as it was not possible to perform delirium screening at any time.

Data collection

Data were collected from September to November 2016. Screening for eligibility was performed on weekdays. Patient characteristics data (age, sex, abuses of nicotine or alcohol, diabetes mellitus, history of vascular disease, hypertension), ICU-related information (APACHE II score ,Acute Physiology and Chronic Health Evaluation II score ,SOFA score), Pittsburgh Sleep Quality Index (PSQI)[15],and hematological indicators (pH,PaO₂,PaCO₂, blood lactate [Lac],white blood cell [WBC] count, hemoglobin [Hb],platelet [PLT],hematocrit [HCT], procalcitonin [PCT],

albumin[ALB], total bilirubin[TBIL], direct bilirubin [DBIL], glutamic-pyruvic transaminase [ALT], glutamic-oxalacetic transaminase[AST], blood urea nitrogen [BUN], creatinine[Cr], uric acid[UA] and electrolyte.),sleep quality, duration of ventilation time, length of ICU stays and length of hospital stays were collected from the electronic patient data management system and through medical chart review, and the time cutoff point is 28 days. The study was approved by the Central South University Xiangya Hospital Ethics Committee.

Assessment of delirium

The experienced ICU clinicians screened patients for delirium two times a day using the Confusion Assessment Method for the ICU (CAM-ICU) as per clinical routine. The criteria that define delirium through the CAM-ICU are as follows: 1. acute change or fluctuating course of mental state; 2. inattention; 3. altered level of consciousness; and 4. disorganized thinking. The presence of delirium is defined by the following composition: 1 + 2 + 3 or 1 + 2 + 4[16]. Patients were classified of having delirium if they had at least one positive CAM-ICU during their ICU stay.

Assessment of diseases type

The subgroup classification is based on the disease system of the included patients. included heart and vascular disease, abdominal disease, pulmonary disease, cerebral disease, maxillofacial/limbs disease, gynecologic and obstetric disease, urinary and spinal disease. Otherwise we used the definition of sepsis 3.0 for sepsis and septic shock [17].

Statistical analysis

Data were processed using SPSS 18.0 software (SPSS, IL, USA). The measurement data were expressed as mean (standard deviation) and analyzed using normality tests. Differences between the groups were analyzed using the t test for normally distributed data and Wilcoxon rank-sum test for unnormal distributed data, which represented by [M (P25, P75,)]. Categorical data between groups was analyzed using the χ^2 test (When the theoretical frequency is < 5, the continuous correction method is adopted. When the theoretical frequency is < 1, the exact probability method is adopted). Kaplan-Meier curves were analyzed by the log-rank test. Survival analysis was performed by multiple stepwise Cox regression model. $P < .05$ and $P < .01$ were considered statistically significant.

Results:

We conducted an observed study of consecutive patients from September to November 2016, who underwent surgical operation or with poor conservative treatment were admitted to the ICU. Of a total of 459 patients were screened in this study, 42 patients met the exclusion criteria and 11 patients did not complete delirium evaluation. Therefore, 406 patients were enrolled in the study after CAM-ICU evaluation was successfully completed. In 406 patients with our study, the primary diseases included heart and vascular disease(n = 107), abdominal disease(n = 107), pulmonary disease(n = 41), sepsis/septic shock(n = 37), cerebral disease(n = 34), maxillofacial/limbs disease(n = 29), gynecologic and obstetric disease(n = 21), urinary(n = 17) and spinal disease(n = 13). (Fig. 1).

Baseline Features and Biochemical Indicators in Patients Between Delirium and Non-delirium Groups

Of these 406 selected patients, 186 (45.8%) presented delirium during ICU stay. the mean ages of the delirium group (n = 186; 101 males) and the non-delirium group (n 220; 135males) were 60 ± 14 and 50 ± 16 years, respectively, and the age between the two groups was statistically significant($P \leq 0.001$). Compared to the non-delirium group, the delirium group patients exhibited a significantly higher APACHE II score (14 ± 6 vs 9 ± 5 ; $P < 0.001$) and SOFA score (8 ± 5 vs 5 ± 4). The delirium group showed bad sleep quality($P \leq 0.001$) and significantly

more history of hypertension (39% vs 25%, $P = 0.003$), MODS (40% vs 21%; $P < 0.001$), sedation (82% vs 65%; $P < 0.001$), and vasoactive drugs use (39% vs 29%; $P = 0.04$). The delirium group also showed longer duration of ventilation (11 hours [3,27] vs 5 hours [1,10]; $P < 0.001$), Length of ICU stay (5.5 ± 5.4 vs 3.0 ± 2.5 ; $P < 0.001$) and higher 28-day mortality (13% vs 4%; $P < 0.001$). (Table 1).

Table 1

Baseline Features and Biochemical Indicators in Patients Between Delirium and Non-delirium Groups

Variables	Delirium (n = 186) n (%)	Non delirium (n = 220) n (%)	P value
Age, mean(SD) ^a , y	60 ± 14	50 ± 16	≪0.001
Men	101(54)	135(61)	0.151
History of hypertension	73(39)	56(25)	0.003
History of cardiac disease	55(30)	48(22)	0.074
Diabetes mellitus	21(11)	18(8)	0.29
History of smoking	48(26)	73(33)	0.105
History of drinking	24(13)	28(13)	0.958
APACHE ^b II score, mean (SD)	14 ± 6	9 ± 5	≪0.001
SOFA ^c score, mean (SD)	8 ± 5	5 ± 4	≪0.001
MODS	75(40)	46(21)	≪0.001
Mechanical ventilation	156(84)	171(78)	0.119
Duration of ventilation, median (IQR) ^d , h	11[3,27]	5[1,10]	≪0.001
Sedation	152(82)	143(65)	≪0.001
Vasoactive drugs	72(39)	64(29)	0.04
Sleep quality assessment(PSQI) ^e			≪0.001
Fairly good	5(3)	57(26)	
Fairly bad	18(10)	80(36)	
Very bad	163(87)	83(38)	
Length of ICU stay, mean (SD), d	5.5 ± 5.4	3.0 ± 2.5	≪0.001
Length of hospital, mean (SD), d	20.5 ± 11.9	19.5 ± 17.2	0.504
28-day mortality	25(13)	9(4)	0.001
PH,mean(SD)	7.37 ± 0.10	7.4 ± 0.1	0.422
PaO ₂ ,mean(SD)	128.6 ± 63.2	135.1 ± 58.1	0.284

^aSD, standard deviation; ^bAPACHE, Acute Physiology, age and chronic Health Evaluation; ^cSOFA, Sequential Organ Failure Assessment; ^dIQR, interquartile range; ^ePSQI, Pittsburgh Sleep Quality Index;

MODS, multiple organ dysfunction syndrome; WBC, white blood cell; Hb, hemoglobin; PLT, platelet; Hct, hematocrit; PCT, procalcitonin; ALB, albumin; TBIL, total bilirubin; DBIL, direct bilirubin; ALT, glutamic-pyruvic transaminase; AST, glutamic-oxalacetic transaminase; BUN, blood urea nitrogen; Cr, creatinine; UA, uric acid.

Variables	Delirium (n = 186) n (%)	Non delirium (n = 220) n (%)	P value
PaCO ₂ ,mean(SD)	128.6 ± 63.3	39.3 ± 14.3	0.787
Lac,mean(SD)	3.3 ± 8.5	2.1 ± 2.7	0.052
WBC,mean(SD)	14.8 ± 6.9	14.2 ± 7.3	0.352
Hb,mean(SD)	96.0 ± 24.3	98.5 ± 23.1	0.285
PLT,mean(SD)	146.5 ± 73.2	162.7 ± 87.9	0.047
Hct,mean(SD)	29.5 ± 7.1	30.6 ± 11.3	0.234
PCT, median (IQR)	2.0[0.2,12.1]	0.9[0.2,4.7]	0.023
ALB,mean(SD)	28.5 ± 5.9	29.6 ± 6.4	0.082
TBIL, median (IQR)	15.3[9.3,31.2]	15.9[10.3,24.3]	0.674
DBIL, median (IQR)	7.2[4.1,14.9]	7.4[4.45,11.15]	0.503
ALT, median (IQR)	22.9[13.5,49]	21.0[13.0,39.4]	0.155
AST, median (IQR)	40.0[24.0,98.0]	38.6[20.7,78.3]	0.091
BUN, median (IQR)	8.5[5.4,12.7]	6.7[4.3,10.2]	0.001
Cr, median (IQR)	110.0[83.0,165.0]	92.0[72.0,123.5]	0.027
UA,mean(SD)	318.6 ± 146.4	297.6 ± 142.5	0.146
^a SD, standard deviation; ^b APACHE, Acute Physiology, age and chronic Health Evaluation; ^c SOFA, Sequential Organ Failure Assessment; ^d IQR, interquartile range; ^e PSQI, Pittsburgh Sleep Quality Index;			
MODS, multiple organ dysfunction syndrome;WBC, white blood cell; Hb, hemoglobin; PLT, platelet; Hct, hematocrit; PCT, procalcitonin; ALB, albumin; TBIL, total bilirubin; DBIL, direct bilirubin; ALT, glutamic-pyruvic transaminase; AST, glutamic-oxalacetic transaminase; BUN, blood urea nitrogen; Cr, creatinine; UA, uric acid.			

In biochemical indicators, compared to the non-delirium group, the delirium group showed significantly higher PCT(2.0[0.2,12.1] vs 0.9[0.2,4.7],P = 0.023), BUN (8.5[5.4,12.7] vs 6.7[4.3,10.2],P=0.001)and Cr(110.0[83.0,165.0] vs 92.0[72.0,123.5],P = 0.027), while PLT(146.5 ± 73.2 vs 162.7 ± 87.9,P = 0.047) was significantly lower. A significant difference was not observed in the other indicators between the two groups (P < 0 .05). (Table 1).

The incidence and risk factors for delirium in different disease types

The overall incidence of ICU delirium was 45.8% (186/406), and the incidence of different diseases is different, from 15% (spine disease) to 68% (cerebral disease). The incidence of delirium was highest in patients with cerebral disease (68%), followed by pulmonary disease (63%), maxillofacial/limbs disease (52%), sepsis/ septic shock (49%), heart and vascular disease (44%) and abdominal disease (42%). (Fig. 2)

A multiple logistic regression was conducted, with delirium as a dependent covariate. The variables that were introduced in the logistic regression model were the result of the univariate analysis that preceded the multivariate

analysis; the variables that were introduced in the model were those that showed a statistically significant relationship at the level of 0.05 ($p < 0.05$) with the dependent variable (occurrence of delirium), we reached the conclusion that for all patients, age, APACHE II score, sedation, and duration of ventilation were independent risk factors for delirium. For example, the older patients are more likely to develop delirium (OR = 1.756, $p = 0.001$), patients who have a higher APACHE II score were more susceptible to develop delirium (OR = 1.093, $p = 0.001$), patients who had longer duration of ventilation were more susceptible to develop delirium (OR = 1.022, $p = 0.012$). In addition, patients who underwent sedation (OR = 3.406, $p = 0.001$) were prone to develop delirium more frequently. While good sleep quality was a protective factor for delirium (OR = 0.186, $p < 0.001$). (Table.2)

However, the risk factors are different for different type of disease. For heart and vascular disease subgroup, only sleep quality (OR = 0.236, $p = 0.001$) was independent risk factor for delirium. For abdominal disease subgroup, age (OR = 2.514, $p = 0.002$), vasoactive drugs (OR = 13.799, $p = 0.002$), and sleep quality (OR = 0.114, $p = 0.001$) were risk factors for the delirium. And for sepsis and septic shock subgroup, age (OR = 1.100, $p = 0.022$), APACHE II scores (OR = 1.255, $p = 0.001$) and sleep quality (OR = 0.090, $p = 0.034$) were risk factors for the delirium. But our study shows no significant risk factor for delirium in lung diseases and cerebral diseases subgroup, which may be related to the reasons for fewer cases. (Table 2)

Table 2

Multivariate regression analysis of risk factors for delirium as dependent variable in all patients and different diseases types

Variables	All patients (n = 406) [P; (OR ^a ,95%CI ^b)]	Heart and vascular disease (n = 104) [P; (OR,95%CI)]	Abdominal disease (n = 92) [P; (OR,95%CI)]	Sepsis/Septic shock (n = 37) [P; (OR,95%CI)]	Cerebral disease (n = 31) [P; (OR,95%CI)]	Pulmonary disease(n = 36) [P; (OR,95%CI)]
Age, y	0.001;(1.756,1.406–2.194)	–	0.002;(2.514,1.397–4.524)	0.022;(1.100,1.014–1.194)	–	–
APACHE II score	0.001;(1.093, 1.039–1.150)	–	–	0.001;(1.255,1.112–1.417)	–	–
Sedation	0.001;(3.406, 1.867–6.212)	–	–	–	–	–
Vasoactive drugs	–	–	0.002;(13.799,2.669–71.361)	–	–	–
Sleep quality assessment (PSQI)	0.001;(0.186, 0.121–0.288)	0.001;(0.236, 0.111–0.500)	0.001;(0.114,0.036–0.366)	0.034;(0.09,0.010–0.829)	–	–
Duration of ventilation	0.012;(1.022,1.005–1.040)	–	–	–	–	–

^aOR, odds ratio; ^b95%CI, 95% confidence intervals; “–” means P has no statistically significant.

The prognosis of delirium in different diseases types

A multivariate stepwise Cox regression model was used to analyze the length of ICU stays and 28 days survival time between delirium and non-delirium groups. Our study found that in all patients group, delirium group exhibited a significantly longer ICU stays ($P < 0.001$) and higher 28-day mortality ($P = 0.001$) than the non-delirium group.

The difference of ICU stays between delirium and non-delirium groups in the subgroup of heart and vascular disease ($P < 0.001$), pulmonary disease ($P = 0.011$), sepsis/septic shock ($P < 0.001$) and cerebral disease ($P = 0.011$) were consistent with the general population. while the differences between the abdominal disease subgroups were insignificant ($P = 0.47$). (Fig. 3)

But the sepsis/septic shock subgroup was the only one whom has the significant difference in 28-day mortality between delirium and non-delirium groups ($P = 0.006$). (Fig. 4)

Discussion

Delirium in the ICU is recognized as a major public health problem. Delirium on the intensive care unit has now come of age. It may not be deadly, but it is still an extremely serious complication that richly deserves its priority status for action and research [18]. Our study showed the delirium has a high incidence in critical patients and is associated with poor prognosis, and the incidence of delirium varied greatly with the type of disease. Age, APACHE II score, sedation, sleep quality and duration of ventilation were independent risk factors for delirium. The risk factors are different for different types of disease, age and sleep quality were independent risk factors for the development of delirium in most subgroup diseases. ICU delirium is associated with worse outcomes including ICU stays and 28-day mortality. the prognosis of delirium was different in different disease types, among them, patients with sepsis/septic shock have the worst prognosis.

First, the overall incidence of ICU delirium of this study was 45.8%, and the incidence of different diseases is different, from 15–68%. Our earlier studies showed that the incidence of delirium in septic populations range between 17.7–42.3% [6,19]. Takako Yamaguchi, R.N. et al [9] found that 27.8% patients developed delirium during the ICU stay in a Japanese intensive care unit. retrospective cohort study showed delirium occurred in 28% of patients who after cardiac surgery. And the incidence of delirium varied greatly with the type of procedure, which was most common in transapical TAVI (47%), and least common in transfemoral TAVI (17%) [10].

Second, our results demonstrated that age, APACHE II score, use of sedatives, sleep disorder and duration of ventilation were independent risk factors for delirium. However, the risk factors are different for different diseases, which may be related to the different injury mechanisms involved in each disease. Although there are various hypotheses concerning the pathogenesis of delirium, the specific pathophysiological mechanisms are unclear [20]. Available data suggest that numerous pathological factors may serve as precipitants for delirium, each having differential effects depending on patient specific patient physiological characteristics (substrate). [8,21,22]. such as Takako Yamaguchi, R.N. et al found that older age and biopsychosocial vulnerability assessed by the Complexity Prediction Instrument (COMPRI) were risk factors of ICU delirium, and ICU delirium was a predictor of increased mortality and associated with prolonged ICU and hospital LOS. length of stay [9]. Harten A E V et al [23] showed that during cardiac surgery maintaining mean arterial pressures of 80–90 mm Hg may reduce the incidence of both postoperative delirium and cognitive dysfunction, which suggest that cerebral hypoperfusion or hypoxia could be a contributing factor to changes in cognition. In addition, this may be related to the small number of cases included in

our study. So, the need for research on this topic on a larger scale is obvious. Recognizing these risk factors is important for physicians to develop preventive strategies to reduce delirium and its negative consequences [8,24].

Overall, in this study, age and sleep disorders are the main independent risk factors for the development of various types of diseases. Pinho et al [25] and Pendlebury et al [26] state that, medically ill older adult patients, with an increased delirium risk from 3% for those less than 65 years old to 14% for those 65 to 74 years old and 36% for patients 75 years and older ($P < .0001$). Multiple studies have found older age to be an independent risk factor for delirium among hospitalized, Pandharipande et al [27] indicates that the incremental risk is large for patients 65 years and older, the probability of transitioning to delirium increased dramatically (by 2%) for each year of life after 65 years. Adjusted OR (odds ratio), 1.01 (95%CI = 1.00, 1.02, $P = 0.03$). Possible mechanisms are as follows: Neuronal loss, Changes in various neurotransmitter systems, Age-related decline in white matter integrity and regional cerebral blood flow, Age-related changes in brain neurochemical activity and so on [28]. Similarly, patients with very bad sleep quality had the highest rate of delirium, which was consistent with lots studies. Maldonado et al [29,30] suggested that disruptions to the 24-hour circadian rhythm cycle, the usual stages of sleep, and variations in natural light exposure may lead to disturbances in the physiological sleep architecture that may contribute to the development of delirium. Madrid et al [31] state that the continuous light, noise, caring activities medications, etc. which contributes to poor sleep quality and delirium by inducing circadian disruption and has a negative impact on human health. There are limited pharmacologic interventions available to treat sleep disturbances in critical illness, however, Knauert et al [32] suggests that multidisciplinary strategies that alter the intensive care unit (ICU) environment and cluster care delivery have shown promise in sleep and circadian promotion and delirium reduction. This is our responsibility to apply the best available, evidence-based medicine to our practice and it is also the direction we need to work hard in the future [33]. Prospective studies with a much greater sample size would be needed in order to determine the causality of certain risk factors for delirium [34,35].

Third, Delirium poses the threat not only of longer-term undesirable outcomes but also high mortality. our results show that for all patients, patients with delirium exhibited a significantly longer ICU stay and higher 28-day mortality, and the prognosis difference between the sepsis/shock patients with delirium and non-delirium is the most significant. This result was consistent with similar findings in studies by Yamaguchi, et al [9] and Svenningsen et al [24]. Our previous study also came up with similar results [6], patients with sepsis associated delirium have higher short-term (28-day) and long-term (6-month) mortality rates. The possibility reason is that the primary disease is relatively serious. In addition, the treatment of sepsis patients requires a long period, and the mechanism of sepsis associated delirium is complicated, appears to involve direct cellular damage to the brain, mitochondrial and endothelial dysfunction, neurotransmission disturbances, and derangements of calcium homeostasis in brain tissue [36]. Pauley et al state, the mortality of delirium which associated with worse survival and greater resource consumption, have highlighted a growing critical care burden in the contemporary medical [34]. Longer stays in the intensive care unit (ICU) can be an opportunistic battlefield where not only is the length of stay longer, but also there is increased time that lapses with the potential for a patient fall, nosocomial infection, urinary tract infection, and other untoward events [33]. The effects of an experience in the ICU that includes delirium can be long lasting and can continue after transfer out of the ICU. which can develop psychological problems and cognitive impairment in survivors [17]. Some studies describe the experience of intensive care patients who have had delirium [18,19].it was difficult for some patients to differentiate between what was real or not. some patients lack of memory for a period in the unit. And some attempts to make sense of the experience of delirium both during and after being in the ICU.

However, there was no difference in 28-day mortality between delirium and non-delirium in other diseases and show different prognostic outcomes. For example, there is no difference in the ICU stay between the delirium or non-delirium patients of abdominal disease, the possible reason for consideration is that the patients with abdominal diseases included in this study were all surgical patients and showed transient delirium, which reversal quickly and has no affection on ICU stay. It is in contrast to what has been demonstrated in Raats et al's study [37] which show that high incidence of delirium was found in abdominal surgery patients. Delirium was associated with adverse outcomes including higher hospital stay, mortality and discharge to a nursing home. Unlike other studies [38,39], there was no significant difference in mechanical ventilation time between delirium and non-delirium patients of pulmonary diseases. The most probable answer for this might be that the patients with pulmonary diseases which our studied included were patients with respiratory failure were ineffective in medical treatment, and the other reason could take for considered is the fact that we had a rather small number of patients with delirium who were documented and analyzed.

Of course, our study had some clinical limitations. First, it was a single-center observational study, and only a rather small number of patients with delirium who were documented and analyzed, such as pulmonary disease, cerebral disease and sepsis/shock. Second, the evaluation time of delirium was twice a day. If the patient's delirium occurs outside the assessment time, it would lead to missed diagnosis. In addition, our study only evaluated short-term prognosis of delirium and did not follow long-term prognosis of patients with delirium, resulting in a less than perfect study.

Conclusions

The incidence of delirium varied greatly with the type of disease. The risk factors for delirium are different for different types of disease, age and sleep quality were independent risk factors for the development of delirium in most subgroup diseases. ICU delirium is associated with worse outcomes including ICU stays and 28-day mortality. The prognosis of delirium was different in different disease types, among them, patients with sepsis/septic shock associated delirium have the worst prognosis. Further research is needed in the field of different disease types in ICU patients to determine the causality and etiology of certain risk factors for delirium.

Abbreviations

CAM-ICU, Confusion Assessment Method for the ICU; CI, confidence interval; ICU, intensive care unit; IQR, interquartile range; RASS, Richmond Agitation Sedation Scale; PSQI, Pittsburgh Sleep Quality Index; MODS, multiple organ dysfunction syndrome; WBC, white blood cell; Hb, hemoglobin; PLT, platelet; HCT, hematocrit; PCT, procalcitonin; ALB, albumin; TBIL, total bilirubin; DBIL, direct bilirubin; ALT, glutamic-pyruvic transaminase; AST, glutamic-oxalacetic transaminase; BUN, blood urea nitrogen; Cr, creatinine; UA, uric acid.

Declarations

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Not available.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

ZLN, AYH, AML,DSY, PQY and FQ contributed to the study conception and design. ZLN, AYH and PQY performed the data analysis and interpretation. FQ, and DSY revised the manuscript for important intellectual content. ZLN, AYH, DSY, PQY and FQ gave final approval of the version to be published. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

All authors consent to publication.

Ethics approval and consent to participate

This study was conducted in line with the standards of medical ethics. It was approved by the Central South University Xiangya Hospital Ethics Committee, and informed consent was obtained from the patients or their families.

References

1. Ely E W, Shintani A, Truman B, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *Jama* 2004; 291(14):1753.
2. Ramoo V, Abu H, Rai V. Educational Intervention on Delirium Assessment Using Confusion Assessment Method-ICU (CAM-ICU) in a General Intensive Care Unit. *J Clin Nurs* 2018.
3. Ely E W, Inouye S K, Bernard G R, et al. Delirium in Mechanically Ventilated Patients: Validity and Reliability of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Jama* 2001; 286(21):2703-2710.
4. Dessap AM, Roche-Campo F, Launay JM, et al. Delirium and Circadian Rhythm of Melatonin During Weaning from Mechanical Ventilation: An Ancillary Study of a Weaning Trial. *Chest* 2015;148(5):1231-1241.
5. Souza-Dantas V C, Póvoa P, Bozza F, et al. Preventive strategies and potential therapeutic interventions for delirium in sepsis. *Hospital Practice* 2016; 44(4):190-202.
6. Feng Q, Ai Y H, Gong H, et al. Characterization of Sepsis and Sepsis-Associated Encephalopathy. *J Intensive Care Med* 2017;(4):885066617719750.
7. Zhang W Y, Wu W L, Gu J J, et al. Risk factors for postoperative delirium in patients after coronary artery bypass grafting: A prospective cohort study. *J Crit Care* 2015; 30(3):606-612.
8. Mori S, Takeda J R, Carrara F S, et al. Incidence and factors related to delirium in an intensive care unit. *Revista Da Escola De Enfermagem Da U S P* 2016; 50(4):587.
9. Yamaguchi T, Tsukioka E, Kishi Y. Outcomes after delirium in a Japanese intensive care unit. *Gen Hosp Psychiatry* 2014;36:634-636.

10. Tse L, Schwarz SK, Bowering JB, et al. Incidence of and Risk Factors for Delirium After Cardiac Surgery at a Quaternary Care Center: A Retrospective Cohort Study. *J Cardiothorac Vasc Anesth* 2015;29:1472-1479.
11. Wang J, Li Z, Yu Y, et al. Risk factors contributing to postoperative delirium in geriatric patients postorthopedic surgery. *Asia Pac Psychiatry* 2015;7:375-382.
12. Ely E W, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med* 2001; 29(7): 1370-1379.
13. Bergeron N, Dubois MJ, Dumont M, et al. Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. *Intens Care Med* 2001; 27(5):859-864.
14. Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med* 2013; 41(1):263-306.
15. Gusmaoflores D, Salluh J I, Chalhub R A, et al. The confusion assessment method for the intensive care unit (CAM-ICU) and intensive care delirium screening checklist (ICDSC) for the diagnosis of delirium: a systematic review and meta-analysis of clinical studies. *Crit Care* 2012; 16(4): 1-10.
16. Dimitri G F, Figueira S J I, Felipe D P, et al. The validity and reliability of the Portuguese versions of three tools used to diagnose delirium in critically ill patients. *Clinics* 2011; 66(11):1917-1922.
17. Seymour C W, Liu V X, Iwashyna T J, et al. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *Jama* 2016; 315(8):762-774.
18. Page VJ, Kurth T. Delirium on the intensive care unit. *BMJ*. 2014;349:g7265.
19. Zhang LN, Wang XT, Ai YH, et al. Epidemiological features and risk factors of sepsis-associated encephalopathy in intensive care unit patients: 2008-2011. *Chin Med J (Engl)* 2012;125(5):828-831.
20. Thorsteinsdottir S A, Sveinsdottir H, Snaedal J. Delirium after open cardiac surgery:systematic review of prevalence, risk factors and consequences. *Laeknabladid* 2015; 101(6):305.
21. Wang J, Li ZW, Yu YM, et al. Risk factors contributing to postoperative delirium in geriatric patients postorthopedic surgery. *Asia-Pacific Psychiatry* 2015; 7(4):375–382.
22. Williams ST. Pathophysiology of encephalopathy and delirium. *J Clin Neurophysiol* 2013;30(5):435-437.
23. Harten A E V, Scheeren T W L, Absalom A R, et al. A review of postoperative cognitive dysfunction and neuroinflammation associated with cardiac surgery and anaesthesia. *Anaesthesia* 2012; 67(3):280-293.
24. Pinho C, Cruz S, Santos A, et al. Postoperative delirium: age and low functional reserve as independent risk factors. *J Clin Anesth* 2015; 33:507-513.
25. Pendlebury S T, Lovett N G, Smith S C, et al. Observational, longitudinal study of delirium in consecutive unselected acute medical admissions: age-specific rates and associated factors, mortality and re-admission. *BMJ Open* 2015; 5(11):e007808.
26. Pandharipande P, Shintani A, Peterson J, et al. Lorazepam Is an Independent Risk Factor for Transitioning to Delirium in Intensive Care Unit Patients. *Anesthesiology* 2006; 104(1):21-26.
27. Maldonado J R. Delirium pathophysiology: An updated hypothesis of the etiology of acute brain failure. *Int J Geriatr Psych* 2017(4).
28. Maldonado J R. Neuropathogenesis of delirium: review of current etiologic theories and common pathways. *Am J Geriatr Psychia* 2013; 21(12):1190-1222.
29. Maldonado J. Pathoetiological model of delirium: a comprehensive understanding of the neurobiology of delirium and an evidence-based approach to prevention and treatment. *Crit Care Clin* 2008; 24(4):789-856.

30. Madrid-Navarro C J, Sanchez-Galvez R, Martinez-Nicolas A, et al. Disruption of Circadian Rhythms and Delirium, Sleep Impairment and Sepsis in Critically ill Patients. Potential Therapeutic Implications for Increased Light-Dark Contrast and Melatonin Therapy in an ICU Environment. *Curr Pharm Design* 2015; 21(24):-.
31. Knauert M P, Haspel J A, Pisani M A. Sleep Loss and Circadian Rhythm Disruption in the Intensive Care Unit. *Clin Chest Med* 2015; 36(3):419.
32. Weinhouse G L. Delirium and sleep disturbances in the intensive care unit: can we do better? *Curr Opin Anaesthesiology* 2014; 27(4):403-408.
33. Pauley E, Lishmanov A, Schumann S, et al. Delirium is a robust predictor of morbidity and mortality among critically ill patients treated in the cardiac intensive care unit. *Am Heart J* 2015; 170(1):79.
34. Volland J, Fisher A, Drexler D. Delirium and Dementia in the Intensive Care Unit: Increasing Awareness for Decreasing Risk, Improving Outcomes, and Family Engagement. *Dimen Crit Care Nurs* 2015; 34(5):259.
35. Theologou S, Giakoumidakis K, Charitos C. Perioperative predictors of delirium and incidence factors in adult patients post cardiac surgery. *Prag & Obser Res* 2018; 9:11-19.
36. Beloborodova N B, Ostrova I V. Sepsis-Associated Encephalopathy (Review). 2017; 13(5):121-139.
37. Raats J W, Steunenbergh S L, Crolla R M, et al. Postoperative delirium in elderly after elective and acute colorectal surgery: A prospective cohort study. *Int J Sur*, 2015, 18:216.
38. Hsieh S J, Soto G J, Hope A A, et al. The Association between Acute Respiratory Distress Syndrome, Delirium, and In-Hospital Mortality in Intensive Care Unit Patients. *Am J Resp & Crit Care Med* 2015; 191(1):71.
39. Aliberti S, Bellelli G, Belotti M, et al. Delirium symptoms during hospitalization predict long-term mortality in patients with severe pneumonia. *Aging Clin & Exp Res* 2015; 27(4):1-9.

Figures

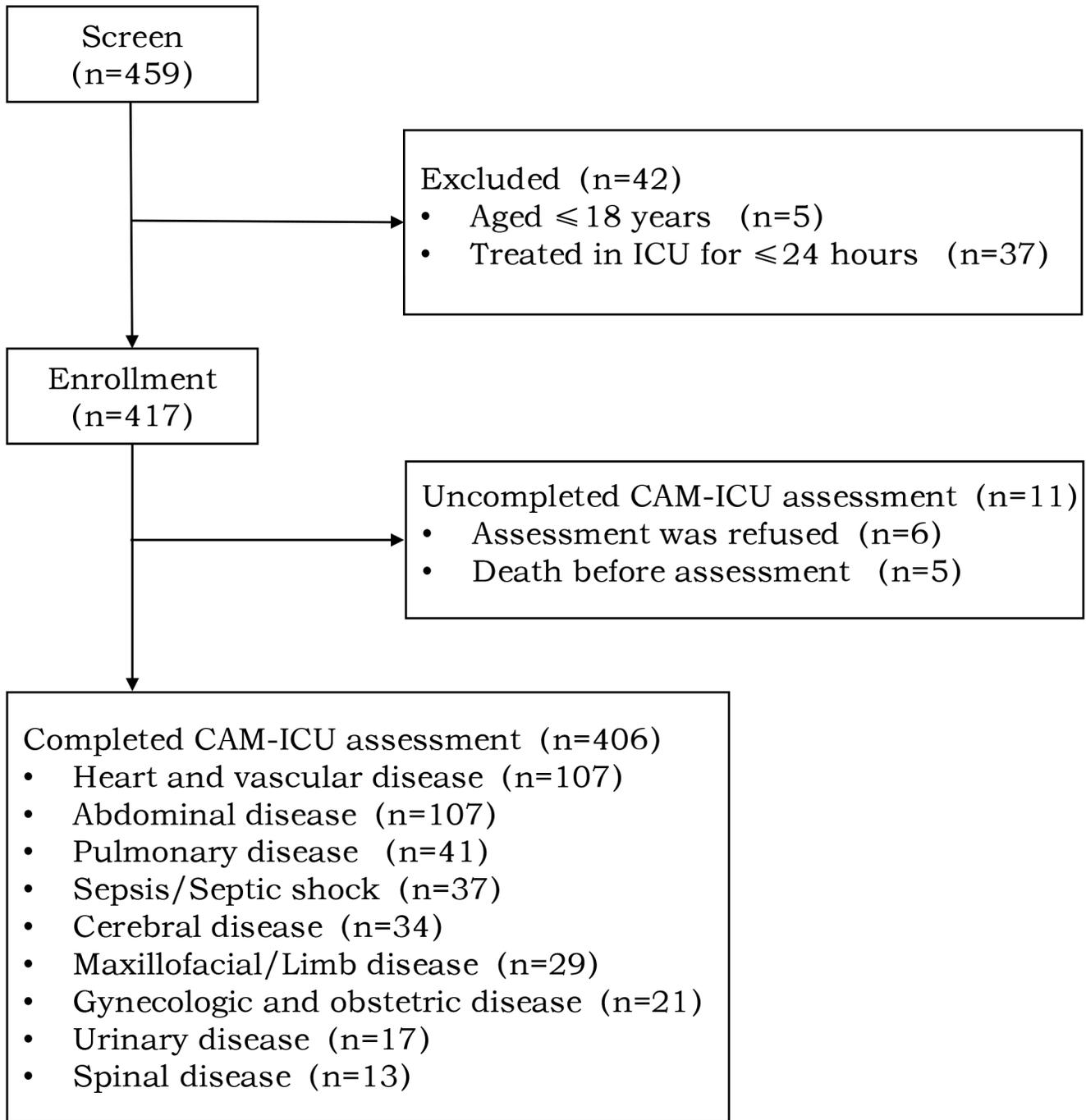


Figure 2

Study flow diagram. 459 patients were screened, of which 42 patients met various exclusion criteria and 11 patients did not complete CAM-ICU assessment. A total of 406 patients were enrolled in our study.

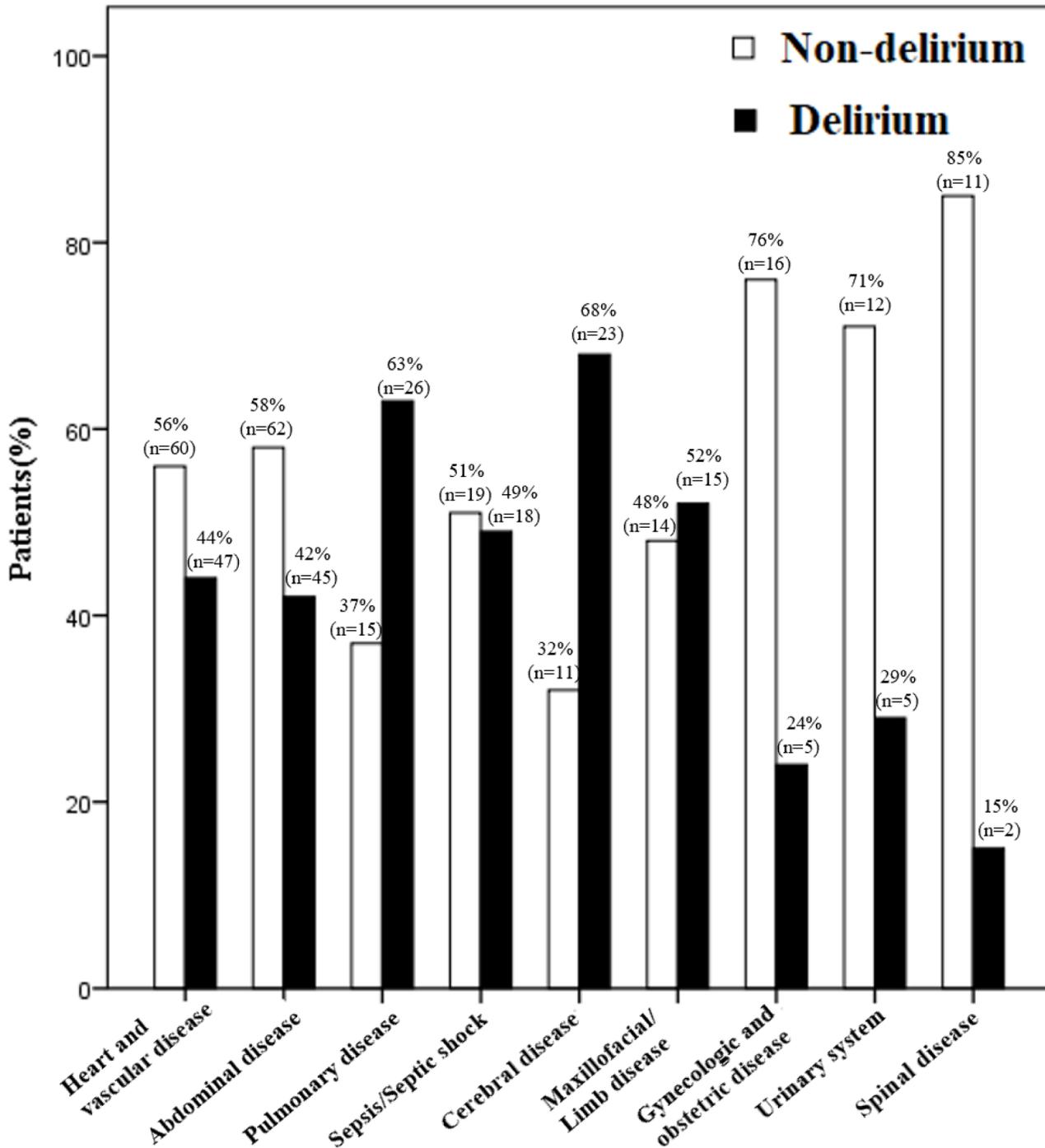


Figure 4

The incidence for delirium in different disease types. The overall incidence of ICU delirium was 45.8% (186/406), and the incidence of different diseases is different, from 15% (spine disease) to 68% (cerebral disease).

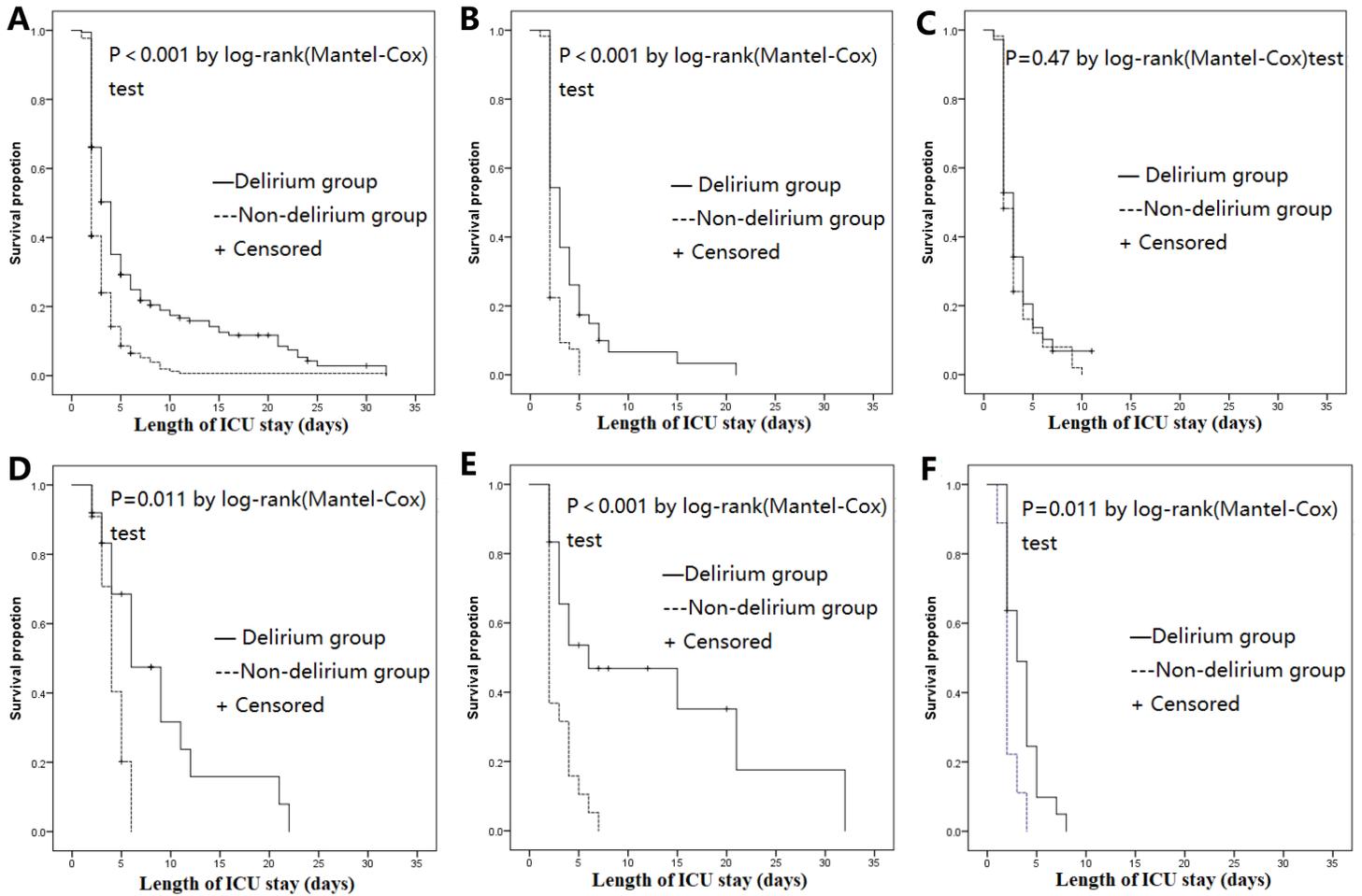


Figure 5

Length of ICU stay between delirium group and non-delirium group in different disease type. A=All of the patients; B= Heart and vascular disease subgroup; C= Abdominal disease subgroup; D= Pulmonary disease subgroup; E= Sepsis/Septic shock subgroup; F= Cerebral disease subgroup.

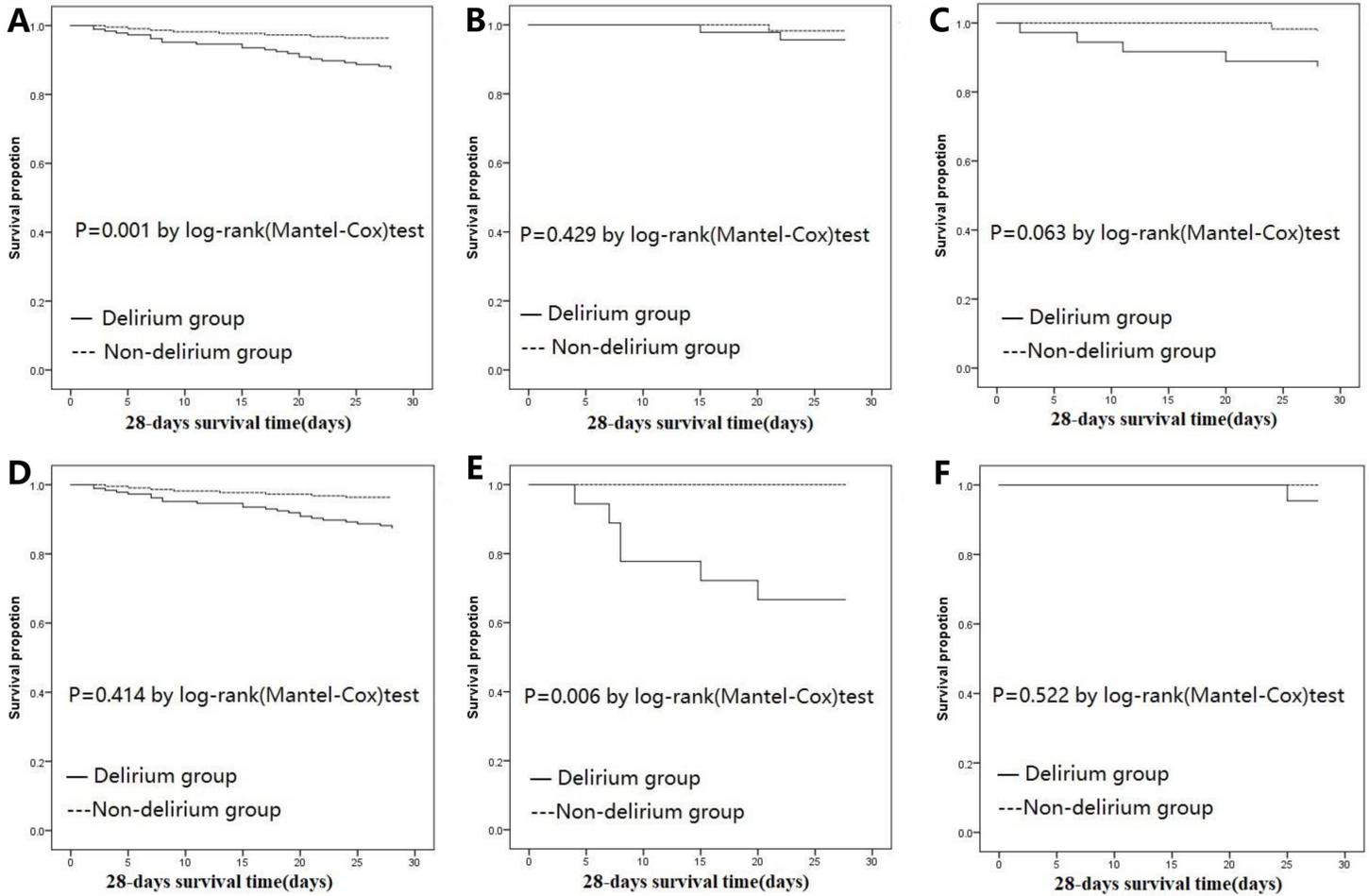


Figure 8

28-day mortality between delirium group and non-delirium group in different disease type. A=All of the patients; B= Heart and vascular disease subgroup; C= Abdominal disease subgroup; D= Pulmonary disease subgroup; E= Sepsis/Septic shock subgroup; F= Cerebral disease subgroup.

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