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Occurrence and predictors of delirium in critically ill older patients: a prospective cohort study

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Abstract

Objectives: This study aims to analyze the occurrence of delirium in critically ill older patients and to identify predictors of delirium.

Methods: This prospective study included critically ill older patients admitted into level II units of Intensive Care Medicine Department of a University Hospital. Patients with Glasgow Coma Scale score ≤11, traumatic brain injury, terminal disease, history of psychosis, blindness/deafness, or inability to understanding/speaking Portuguese were excluded. The Confusion Assessment Method-Short Form (CAM-4) was used to assess the presence of delirium.

Results: The final sample (n = 105) had a median age of 80 years, most being female (56.2%), widowed (49.5%), and with complete primary education (53%). Through CAM-4, 36.2% of the patients had delirium. The delirium group was more likely to have previous cognitive decline (48.6% vs 19.6%, $P = .04$) and severe dependency in instrumental activities of daily living (34.3% vs 14.8%, $P = .032$), comparing with patients without delirium. The final multiple logistic regression model explained that patients with previous cognitive decline presented a higher risk for delirium (odds ratio: 4.663, 95% confidence Interval: 1.055–20.599, $P = .042$).

Conclusions: These findings corroborate previous studies, showing that cognitive decline is an independent predictor for delirium in older patients. This study is an important contribution for the knowledge regarding the predictors of delirium. The recognition of these factors will help to identify patients who are at high risk for this syndrome and implement early screening and prevention strategies. However, further studies with larger samples, recruited from other clinical settings as well as analyzing other potential factors for delirium, will be needed.

Keywords: delirium, aged, risk factor, cognitive decline

Introduction

Delirium represents a common neuropsychiatric syndrome, especially in the hospitalized older population, affecting 18% to 64% of this population,[1] depending on the clinical setting. A recent meta-analysis[2] concluded that the overall prevalence of delirium in hospitalized older people was 33%. The highest rates of delirium are observed in the palliative care units, followed by intensive care unit (ICU) and postoperative setting. In the first case, delirium can affect 85% of end-of-life patients.[1] In the ICU, the incidence of delirium ranges from 20 to 80%,[3,4] and in the postoperative setting, delirium is the most common complication in surgical patients, with an incidence of 15% to 25% after major elective surgery and around 50% after high-risk procedures, such as repairing a hip fracture or cardiac surgery.[5]

According to Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5),[6] delirium is defined by disturbances in attention, awareness, and cognition that are not explained by another preexisting, established, or evolving neurocognitive disorder and that do not occur in the context of a severely reduced level of arousal, such as coma. These disturbances usually begin over a few hours or a few days and tend to fluctuate in severity during the day. Delirium can be caused by a medical condition, an intoxication or withdrawal syndrome, or, mostly, by multiple etiologies.

Delirium is one of the most serious and lethal complications during hospitalization, being associated with poor prognosis and multiple adverse outcomes. Several studies have reported delirium as an independent factor for increased mortality during hospitalization and after discharge,[7,8] longer hospital stay,[9] higher readmission rates,[10] patient falls,[11] and nursing home admission.[12] This syndrome is also a well-established risk factor for both development of dementia and worsening a preexisting dementia.[13-15] Therefore, it determines a significantly increase of health care use and costs[16] as well as an economic burden[17] and a significant psychological distress for the patients and their caregivers.[18,19]

Nevertheless, this syndrome is underrecognized and often poorly treated by health professionals, which can worsen the

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associated negative outcomes. Nondetection rates around 60% have been reported,[20] with several factors contributing to this, such as the fluctuating course of delirium and its frequent overlap with dementia and depression.[14]

Similar to other geriatric syndromes, delirium is usually multifactorial in older persons, resulting from several predisposing factors intrinsic to the patient who make the person more vulnerable to precipitating factors, during hospitalization.[1] According to this model, patients with several predisposing factors are highly susceptible to delirium, even being exposed to a minor precipitating factor. This explains the reason why older people are a high-risk group for the development of delirium. On the other hand, in a healthy patient, delirium will only develop through continued exposure to several precipitating factors. The more predisposing factors are present, the less precipitating factors are needed to lead to the onset of delirium.[21] Therefore, it is crucial to understand which factors are associated with this neuropsychiatric syndrome.

Despite this well-established multifactorial model, risk factors may change according to the clinical setting. Dementia or cognitive decline, functional impairment, visual deficit, comorbidity burden, history of alcohol abuse, and advanced age (older than 70 years) are reported as the most common predisposing factors for delirium in both medical and noncardiac surgery populations.[1] Precipitating factors tend to vary more depending on the patient population. For example, in medical patients, polypharmacy, psychoactive medication use, physical restraint, and the use of bladder catheter are very frequent. In the ICU, the consumption of psychoactive medication, trauma admission, and neurosurgery are commonly reported.

Bearing this in mind, this study aims to analyze the occurrence of delirium in critically ill older patients admitted in level II units (known as intermediate care units) of an Intensive Care Medicine Department in a University Hospital. This study also aims to identify predictors associated with the development of delirium in these patients.

Methods

Sample recruitment

This study is part of a larger prospective cohort research project called: "Impact of Delirium on Older Adult Patients, Family and Staff," funded by the Foundation for Science and Technology (FCT) [Grant No. SFRH/BPD/103306/2014], which has as main objective to analyze the experience of delirium and related psychological distress in older patients, their families, and nurses.

In this context, between September of 2017 and July 2018, a sample of critically ill older patients was consecutively recruited from Level II units of the Intensive Care Medicine Department (ICMD) of the Centro Hospitalar Universitário São João (CHUSJ), in Porto (Portugal). The Level II units are high dependency units for patients who need multiorgan monitoring and support for only one organic function, without invasive mechanical ventilation required.[22] Patients with a total score of ≤11 on the Glasgow Coma Scale (GCS) score,[23] admitted with traumatic brain injury, having terminal disease, history of psychosis, with blindness and/or deafness, or difficulty in understanding and/or speaking Portuguese fluently were excluded.

This study and manuscript were conducted according to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines statement.[24]

Ethical considerations

The research project was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee for Health of the Hospital where this study was performed. All included participants had to sign a written informed consent agreeing to participate in this study. In patients who were unable to give their consent, this was obtained through a close family member. For patients who developed delirium, consent was also taken after its resolution. Data collected were codified to ensure data protection and confidentiality.

Procedures

After informed consent, a researcher psychologist collected data about the previous cognitive and functional status of the patient, using the Informant Questionnaire on Cognitive Decline in the Elderly-Short Form (IQCODE-SF),[25] Barthel Index (BI),[26] and Lawton Index (LI).[20]

The IQCODE-SF[25] is a screening tool to assess for possible cognitive decline and dementia in older people. It is a structured interview to be completed based on family and/or caregiver information to understand whether there have been cognitive changes over time (in the past 2 years) in the older person. IQCODE-SF includes 16 items, rated on a 5-point Likert scales (1—strongly disagree, 2—disagree, 3—neither agree nor disagree, 4—agree, and 5—strongly agree). The cut-off scores are based on the total score, which is divided by the number of questions (range 1–5). The presence of cognitive decline is established by a total score ˃3.44.

The degree of dependence of patients in Basic Activities of Daily Living (BADL) was assessed with the BI,[26] an ordinal scale used to measure performance in the following ten BADL: feeding, personal toileting, bathing, dressing and undressing, getting on and off a toilet, controlling bladder, controlling bowel, moving from wheelchair to bed and returning, walking on level surface (or propelling a wheelchair if unable to walk), and ascending and descending stairs, which are scored over three levels (independence, need help, dependent). The total score may range between 0 and 100 points. In this study, the Portuguese cut-off points, such as total dependence (<20 points), severe dependence (20-39) moderate dependence (40–59), mild dependence (60–89), and independence (90–100), were considered.[27]

In addition, LI[20] was applied as an assessment tool to evaluate eight Instrumental Activities of Daily Living (IADL), specifically ability to use telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for own medications, and ability to handle finances. Each IADL is scored from 1 to 3/4 or 5, where the highest score corresponds to a greater degree of dependency and the total score ranges between 8 and 30. The Portuguese cutoffs were also used in this study: 8 (independence), 9 to 20 (moderate dependence), and ˃20 (severe dependence).[27] The BI and LI were completed based on information provided by the patient's family.

In what concerns to delirium assessment, all included patients were assessed in the first 24 hours after admission and daily until the moment of discharge by the medical doctors of the research team. This assessment was done with the European Portuguese version of the Confusion Assessment Method-Short Form (CAM-4),[28,29] which assesses the presence of four cardinal features of delirium: (1) acute onset and fluctuating course, (2) inattention, (3) disorganized thinking, and (4) altered level of consciousness. Delirium is suggested if features (1) and (2) and either (3) or (4) are

present. The CAM-4 was completed based on a brief clinical interview, hospital records data review, and information provided by family and/or health staff.

Based on these assessments, patients were divided into two groups: (1) with delirium: patients met complete CAM-4 criteria for delirium (prevalent: present at admission or incident: develop during hospitalization in Level II units) and did not present delirium at the time of unit discharge or (2) without delirium: patients did not present delirium criteria at any time of hospitalization.

Sociodemographic and clinical data, including the Charlson Comorbidity Index (CCI),[30] were collected through the hospital records and clinical interview. In addition, the Acute Physiology and Chronic Health Evaluation II (APACHE-II) and the Simplified Acute Physiology Score II (SAPS-II) were registered, for acute illness severity assessment.

Statistical analysis

The SPSS version 27.0 for Windows (SPSS, Inc, Chicago, IL) was used to perform the statistical analysis of this study.

Patient characteristics were presented as raw frequencies and percentages for categorical variables and as mean and standard deviation (SD) for continuous variables, when normality could be assumed or median and range if normality was not assumed.

Differences between the patients with and without delirium (based on CAM-4 scoring) regarding the sociodemographic and clinical variables collected were analyzed with nonparametric statistical tests, as the data did not assume a normal distribution.

In this analysis, the Mann-Whitney *U* test was used for continuous variables, the chi-square test was used for categorical variables, and the Fisher exact test was used for dichotomous variables, at a significance level of 0.05.

The following sociodemographic variables were considered in this analysis: age, the number of years of schooling (continuous variables), and sex (dichotomous variable). The total score of CCI, the number of total daily medications, the number of comorbidities, the total score of APACHE-II and SAPS-II, the ICMD and hospital length of stay (LoS) (continuous variables), and the total score of IQCODE-SF, BI, and LI (continuous and categorical variables) were included as clinical variables.

Odds ratio (OR) and its 95% confidence interval (CI) were calculated to identify independent predictors of delirium. Variables previously associated with this outcome (eg, LI, IQCODE-SF) in the univariate analyses and other characteristics considered clinically relevant (eg, age, medication, comorbidity) were included in a multiple logistic regression model to identify significant and independent predictors of delirium.

Results

Sociodemographic and clinical characteristics of the older adults

The final sample includes 105 patients, with a median age of 80 (range: 65–103) years. Most were female (56.2%), widowed (49.5%), and with complete primary education (53%). The main reason for admission was respiratory problems (23.8%), followed by postoperative (19%) and cardiac conditions (17.1%). The median APACHE-II and SAPS scores were 15 (minimum: 6, maximum: 32) and 35 (min. = 18, max. = 69), respectively.

According to the CAM-4, 36.2% (n = 38) of patients developed delirium (Table 1). Regarding preadmission clinical data of these patients, the median CCI was 7, ranging between 3 and 15. In addition, the median (min–max) number of comorbidities and daily medication were 4 (1–11) and 6 (1–14), respectively (Table 1). Regarding preadmission cognitive and functional status, 31.4% of the patients had cognitive decline and 22.5% presented severe dependence for IADL, assessed by LI. The median total score of LI was 14, which means moderate dependence (with a minimum value of 8 and a maximum value of 30). Using BI, 77.5% of patients were defined as independent for BADL, and a median value of 100.00 (min. 5–max. 100) was found, which represents independence for the performance of these basic activities (Table 1). The ICMD and hospital LoS median were 4 (range: 1–16) and 13 (range: 3–79) days, respectively.

Differences between patients with and without delirium

With respect to sociodemographic characteristics, no statistically significant differences between patients with and without delirium were found (Table 1).

Regarding clinical data, total scores of CCI, comorbidities, and daily medication did not differ significantly between groups.

However, significant differences in the preadmission cognitive status were found. Patients who develop delirium had a higher median score on the total of IQCODE-SF (median = 3.6 vs 3.0, $P = .015$), comparing with patients who did not. In addition, a higher percentage of patients with delirium than those without presented preexisting cognitive decline (48.6% vs 19.6%, $P = .04$). Regarding the preadmission functional status, significant differences were also found between the two groups, with delirium patients showing more severe dependency in IADL (34.3% vs 14.8%, $P = .032$) (Table 1).

Acute illness severity assessed by APACHE-II and SAPS-II was also higher in patients with delirium (median 17 vs 14, $P = .015$; 38 vs 33, $P = .002$, respectively), reflecting more severe acute conditions with higher mortality risk. The hospital LoS median was higher in delirium group (18.5 vs 11 days; $P = .002$), but no differences were found for ICMD LoS.

Regression model of predictors of delirium

A multiple logistic regression model to identify predictors of delirium was performed. The final model included the following variables: age, comorbidity (CCI), IADL dependence (LI), and cognitive decline (IQCODE-SF). According to this model, patients with previous cognitive decline presented a significantly higher risk of developing delirium (OR: 4.663, 95% CI: 1.055–20.599, $P = .042$) (Table 2).

Discussion

In this prospective study, the rate of occurrence of delirium in critically ill older patients admitted into Level II units was 36.2%. This result is similar to those (20%–41%) found in previous studies by this research team[29,31] and by other groups in this type of units.[32,33]

Critically ill older patients with delirium were more likely to have previous cognitive decline and dependence for IADL, when compared with patients without delirium. The association between preadmission functional status (dependence on IADL) and the consequent development of delirium has already been identified in former studies.[34-36] According to some authors,[37,38] a high level of dependency in older patient is usually related with their frailty, commonly caused by changes of general health

Table 1

Sociodemographic and clinical characteristics of the older adults

Characteristics	Overall		Delirium		No delirium		*P*
	N =105		N = 38		N = 67		
Sociodemographic data							
Age (y), median (min.–max.)		80.0 (65–103)		81.0 (65–103)		78.0 (65–87)	.072*
S n (%)							.279†
Female	59 (56.2)		24 (63.2)		35 (52.2)		
Male	46 (43.8)		14 (36.8)		32 (47.8)		
Education (years), median (min.-max.)		4.0 (0–17)		4.0 (0–17)		4.0 (0–17)	.373*
Clinical Data							
Charlson Comorbidity Index, median (min.-max.)		7.0 (3–15)		8.0 (4–12)		7.0 (3–15)	.109*
Total of comorbidities, median (min.-max.)		4.0 (1–11)		4.0 (1–9)		4.0 (1–11)	.215*
Total of medication (daily), median (min.-max.)		6.0 (1–14)		5.0 (1–13)		5.0 (1–12)	.176*
Preadmission cognitive status							
IQCODE-SF, median (min.-max.)		3.1 (2.7–4.9)		3.6 (3.00–4.93)		3.0 (2.75–4.25)	**.015***
No cognitive decline n (%)	59 (68.6)		18 (51.4)		41 (80.4)		**.04***
Cognitive decline n (%)	27 (31.4)		17 (48.6)		10 (19.6)		
Preadmission functional status							
Lawton Index, median (min.-max.)		14.0 (8–30)		18.0 (8–30)		12.0 (8–29)	**.001***
Independence to moderate dependent n (%)	69 (77.5)		23 (65.7)		46 (85.2)		**.032†**
Severe dependence n (%)	20 (22.5)		12 (34.3)		8 (14.8)		
Barthel Index, median (min.-max.)		100.0 (5–100)		95.0 (40–100)		100.0 (65–100)	.186*
Independence n (%)	69 (77.5)		25 (71.4)		44 (81.5)		.267†
Dependence n (%)	20 (22.5)		10 (28.6)		10 (18.5)		

Min.–Minimum, Max–Maximum; Bold values significant at $P < .05$.
* Mann-Whitney *U* test.
† Chi-square independent test.

status, cognitive impairment, or chronic illnesses, which have also been pointed as predisposing factors for delirium.[1]

To identify independent predictors of delirium, a multiple logistic regression model was performed. Initial analyses of the multiple regression model included not only variables previously associated with delirium but also other characteristics considered clinically relevant. However, because the results were similar with or without the inclusion of these characteristics, the most simplified model was assumed, which included age, CCI, dependence on IADL, and presence of cognitive decline. Based on this model, only the preexistence of cognitive decline was an independent and significant predictive factor for delirium. This result reinforces the hypothesis that delirium and dementia commonly coexist, with the preexisting cognitive decline being a leading predictor of delirium consistently identified across several clinical settings, such as ICU,[35,39] postoperative setting,[40,41] and nursing homes.[42] This finding is also in line with the data of previous systematic reviews and meta-analysis.[43-45] For example, Fong et al[14] concluded that when cognitive impairment or dementia is present at baseline, the risk of delirium increases by 2-fold to 5-fold and outcomes are worsened.

In accordance with some authors,[46,47] the vulnerability of the brain of patients with cognitive impairment or dementia associated with the possible existence of acute medical illnesses and the effects of medication, as well as the environmental factors, leads to a greater predisposition to the development of delirium. Similarly, Fong et al[14] refer that delirium may reflect an uncompensated cognitive state due to stress conditions and may reflect a decline of cognitive reserve. These authors also state that delirium can help to identify people vulnerable to cognitive decline because of genetic predisposition or the presence of an unrecognized dementia. On the other hand, severe precipitating factors of delirium, such as prolonged hypoglycemia or hypoxemia, may cause permanent neuronal damage, increasing the risk of permanent cognitive impairment and new-onset of dementia, as well as acceleration of a preexisting dementia.[46,48,49]

Table 2

Regression model of predictors of delirium

Characteristics	OR (95% CI)	*P*
Age (y)	1.041 (0.949–1.143)	.393
Charlson Comorbidity Index (score)	1.158 (0.915–1.466)	.222
Lawton Index (severe dependence vs independence/ moderate dependence)	1.593 (0.286–8.883)	.595
IQCODE-SF (cognitive decline vs no cognitive decline)	**4.663 (1.055–20.599)**	**.042***

* Bold values significant at $P < .05$.
OR = odds ratio; 95% CI = 95% confidence interval.

The results of the present work reinforce the need for an early identification of older persons with cognitive deficits that has already been highlighted by international guidelines.[50] According to this, all older people admitted to hospital or in long-term care units should be screened for risk factors of delirium and cognitive impairment, using a brief cognitive test (eg, the Mini-Mental State Examination [MMSE]). If recent changes or fluctuations in cognitive and physical functions are identified in people at risk, a clinical assessment should be conducted based on standardized diagnosis criteria or on the CAM short form, by a trained health care professional.

The knowledge about predictors of delirium is extremely important because it allows the identification of patients who are at higher risk and the implementation of early screening and preventive approaches, which may contribute to decrease delirium occurrence.

Strengths and limitations

This study has important strengths and some limitations. First, this study seems as an important contribution to the deepening of the knowledge about predictive factors of delirium in older

persons. Second, this study included a sample of critically ill older patients hospitalized in a clinical setting (level II intermediate units), which has been very little studied, in contrast to intensive care units (level III). However, this study was conducted only in two level II units of the same hospital, which limits the generalizability of these findings. Another limitation is related to the fact that other possible predictors (such as visual/hearing impairment and history of alcohol abuse) of delirium were not considered in the current work.

Conclusions

To conclude, in this study, the cognitive decline was found to be an independent predictor of delirium in older patients admitted to level II units, suggesting that its recognition on admission would be paramount to identify patients who are at higher risk for delirium, and to implement timely screening and preventive interventions. Further studies are needed, with larger samples and in different clinical settings, analyzing the role of this and other relevant potential predictive factors of delirium development and their interaction.

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References

[1] Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet. 2014;383:911–22.
[2] Gibb K, Seeley A, Quinn T, et al. The consistent burden in published estimates of delirium occurrence in medical inpatients over four decades: a systematic review and meta-analysis study. Age Ageing. 2020;49: 352–60.
[3] Dubois MJ, Bergeron N, Dumont M, Dial S, Skrobik Y. Delirium in an intensive care unit: a study of risk factors. Intensive Care Med. 2001;27: 1297–304.
[4] Salluh JI, Wang H, Schneider EB, et al. Outcome of delirium in critically ill patients: systematic review and meta-analysis. BMJ. 2015;350:h2538.
[5] Marcantonio ER. Postoperative delirium: a 76-year-old woman with delirium following surgery. JAMA. 2012;308:73–81.
[6] Association AP. Diagnostic and Statistical Manual of Mental Disorders (DSM-5®). Arlington: American Psychiatric Publishing; 2020.
[7] Witlox J, Eurelings LS, de Jonghe JF, Kalisvaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis. JAMA. 2010;304:443–51.
[8] McCusker J, Cole M, Abrahamowicz M, Primeau F, Belzile E. Delirium predicts 12-month mortality. Arch Intern Med. 2002;162:457–63.
[9] McCusker J, Cole MG, Dendukuri N, Belzile E. Does delirium increase hospital stay? J Am Geriatr Soc. 2003;51:1539–46.
[10] Uthamalingam S, Gurm GS, Daley M, Flynn J, Capodilupo R. Usefulness of acute delirium as a predictor of adverse outcomes in patients >65 years of age with acute decompensated heart failure. Am J Cardiol. 2011;108: 402–8.
[11] Lakatos BE, Capasso V, Mitchell MT, et al. Falls in the general hospital: association with delirium, advanced age, and specific surgical procedures. Psychosomatics. 2009;50:218–26.
[12] Eeles EMP, Hubbard RE, White SV, O'Mahony MS, Savva GM, Bayer AJ. Hospital use, institutionalisation and mortality associated with delirium. Age Ageing. 2010;39:470–5.
[13] Davis DH, Muniz Terrera G, Keage H, et al. Delirium is a strong risk factor for dementia in the oldest-old: a population-based cohort study. Brain. 2012;135(Pt 9):2809–16.
[14] Fong TG, Davis D, Growdon ME, Albuquerque A, Inouye SK. The interface between delirium and dementia in elderly adults. Lancet Neurol. 2015;14:823–32.
[15] Morandi A, Bellelli G. Delirium superimposed on dementia. Eur Geriatr Med. 2020;11:53–62.
[16] Caplan GA, Teodorczuk A, Streatfeild J, Agar MR. The financial and social costs of delirium. Eur Geriatr Med. 2020;11:105–12.
[17] Vasilevskis EE, Chandrasekhar R, Holtze CH, et al. The cost of ICU delirium and coma in the intensive care unit patient. Med Care. 2018;56:890–7.
[18] Martins S, Pinho E, Correia R, et al. What effect does delirium have on family and nurses of older adult patients? Aging Ment Health. 2018;22:903–11.
[19] Williams ST, Dhesi JK, Partridge JSL. Distress in delirium: causes, assessment and management. Eur Geriatr Med. 2020;11:63–70.
[20] Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist. 1969;9:179–86.
[21] Marcantonio ER. Delirium in hospitalized older adults. N Engl J Med. 2017;377:1456–66.
[22] Waydhas C, Herting E, Kluge S, et al. Intermediate care units: recommendations on facilities and structure. Med Klin Intensivmed Notfallmed. 2018;113:33–44.
[23] Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet. 1974;2:81–4.
[24] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg. 2014;12:1495–9.
[25] Jorm AF. A short form of the informant Questionnaire on cognitive decline in the elderly (IQCODE): development and cross-validation. Psychol Med. 1994;24:145–53.
[26] Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. Md State Med J. 1965;14:61–5.
[27] Sequeira C, Sousa L. Cuidar de Idosos com dependência Física e Mental. 2a edição. Lisboa: LIDEL; 2018.
[28] Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann Intern Med. 1990;113:941–8.
[29] Martins S, Lourenço C, Pinto-de-Sousa J, et al. Validation study of the European Portuguese version of the confusion assessment method (CAM). Int Psychogeriatr. 2015;27:777–84.
[30] Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol. 1994;47:1245–51.
[31] Martins S, Moldes P, Pinto-de-Sousa J, et al. Pilot study on the European Portuguese version of the confusion assessment method. Acta Neuropsychiatr. 2014;26:321–4.
[32] González J, Barros J. Delirium in patients of an intermediate care unit: prospective study. Rev Med Chil. 2000;128:75–9.
[33] Mariz J, Santos NC, Afonso H, et al. Risk and clinical-outcome indicators of delirium in an emergency department intermediate care unit (EDIMCU): an observational prospective study. BMC Emerg Med. 2013;13:2.
[34] Dylan F, Byrne G, Mudge AM. Delirium risk in non-surgical patients: systematic review of predictive tools. Arch Gerontol Geriatr. 2019;83: 292–302.
[35] Kalimisetty S, Askar W, Fay B, Khan A. Models for predicting incident delirium in hospitalized older adults: a systematic review. J Patient Cent Res Rev. 2017;4:69–77.
[36] Newman MW, O'Dwyer LC, Rosenthal L. Predicting delirium: a review of risk-stratification models. Gen Hosp Psychiatry. 2015;37:408–13.
[37] Quinlan N, Marcantonio ER, Inouye SK, Gill TM, Kamholz B, Rudolph JL. Vulnerability: the crossroads of frailty and delirium. J Am Geriatr Soc. 2011;59(suppl 2):S262–8.
[38] Eeles EM, White SV, O'Mahony SM, Bayer AJ, Hubbard RE. The impact of frailty and delirium on mortality in older inpatients. Age Ageing. 2012;41: 412–6.
[39] Zaal IJ, Devlin JW, Peelen LM, Slooter AJ. A systematic review of risk factors for delirium in the ICU. Crit Care Med. 2015;43:40–7.
[40] Watt J, Tricco AC, Talbot-Hamon C, et al. Identifying older adults at risk of delirium following elective surgery: a systematic review and meta-analysis. J Gen Intern Med. 2018;33:500–9.
[41] Lee SJ, Jung SH, Lee SU, Lim JY, Yoon KS, Lee SY. Postoperative delirium after hip surgery is a potential risk factor for incident dementia: a systematic review and meta-analysis of prospective studies. Arch Gerontol Geriatr. 2020;87:103977.

[42] Lee J. Risk factors for nursing home delirium: a systematic review. J Korean Gerontological Nurs. 2020;22:75–83.
[43] Ahmed S, Leurent B, Sampson EL. Risk factors for incident delirium among older people in acute hospital medical units: a systematic review and meta-analysis. Age Ageing. 2014;43:326–33.
[44] Pendlebury ST, Lovett NG, Smith SC, Wharton R, Rothwell PM. Delirium risk stratification in consecutive unselected admissions to acute medicine: validation of a susceptibility score based on factors identified externally in pooled data for use at entry to the acute care pathway. Age Ageing. 2017;46:226–31.
[45] Ryan DJ, O'Regan NA, Caoimh R, et al. Delirium in an adult acute hospital population: predictors, prevalence and detection. BMJ Open. 2013;3:e001772.
[46] Wilson JE, Mart MF, Cunningham C, et al. Publisher correction: delirium. Nat Rev Dis primers. 2020;6:94.
[47] Inouye SK. Delirium in older persons. N Engl J Med. 2006;354:1157–65.
[48] Maclullich AM, Anand A, Davis DH, et al. New horizons in the pathogenesis, assessment and management of delirium. Age Ageing. 2013;42:667–74.
[49] Fong TG, Tulebaev SR, Inouye SK. Delirium in elderly adults: diagnosis, prevention and treatment. Nat Rev Neurol. 2009;5:210–20.
[50] National Clinical Guideline C. National Institute for Health and Clinical Excellence: Guidance. Delirium: Diagnosis, Prevention and Management. London: Royal College of Physicians (UK) Copyright © 2010, National Clinical Guideline Centre—Acute and Chronic Conditions; 2010.