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Original Contribution

Incidence and risk factors of postoperative delirium after surgery in the spanish population: The DELPO study

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HIGHLIGHTS

- Multicenter study identifies national incidence of postoperative delirium in Spain.
- Delirium linked to poor outcomes, including extended hospital stays and mortality.
- Findings emphasize the need for early detection and targeted treatment strategies.
- Early risk identification can prevent adverse events and improve surgical outcomes.

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ABSTRACT

Background: Postoperative delirium increases morbidity, mortality, hospital stays, and costs, though 30–40 % of cases are preventable. This study assessed early delirium incidence in 2442 surgical patients across 43 Spanish hospitals, analyzing it by surgery type and related factors. Conducted from November 14 and 21, 2023, with follow-ups on days 2 and 60, it provides insights into factors influencing postoperative delirium and outcomes.
Methods: The study included three phases: (1) recruitment and assessment of surgical patients on November 14 and 21, 2023, across all centers; (2) monitoring for delirium by postoperative day 2; and (3) a follow-up at 60 days. Delirium was diagnosed using the CAM, CAM-ICU, and 4AT scales. The sample size was estimated and multivariable logistic regression and Cox regression analysis were performed to identify independent risk factors and assess the impact of delirium on mortality.
Results: A total of 2442 surgical patients were recruited, mainly male (51.9 %), with a mean age of 76 ± 16 years. The delirium incidence was 3.93 %, with four preoperative independent risk factors identified through multivariate analysis.: Patient age (odds ratio (OR) 1.05, 95 % CI 1.04 to 1.08, $p > 0.001$), cognitive impairment (SBT > 6 points) (OR 1.12, 95 % CI 1.08 to 1.15, $p < 0.001$), substance use disorder (SUD) (OR 3.97, 95 % CI 1.05 to 14.93, $p = 0.042$) and alcoholism (OR 1.92, 95 % CI 1.20 to 3.07, $p = 0.006$), with a model AUROC of 0.81 (95 % CI 0.76 to 0.85). Postoperative delirium was associated with longer hospital stays and significantly higher mortality at 60 days (8.3 % vs 0.6 %).
Conclusion: This Spanish study found that postoperative delirium, linked to longer hospital stays and higher mortality, requires early detection and prevention to improve outcomes.

1. Introduction

Postoperative delirium (POD) is a clinical syndrome defined as an acute and fluctuating alteration of mental status, characterized by a decline in attention and an altered or additional cognitive deficit [1,2]. In the general surgical population, the estimated incidence typically ranges from 2 % to 3 %, but can surge to as high as 50–70 % in high-risk patient groups [3]. Patients undergoing gastrointestinal surgery have a delirium rate of 15–35 % [4], which can increase to 45.8 % in patients undergoing cardiac surgery [5–7]. In elective orthopedic procedures the rate is around 13–61 % [8], with an incidence of 2.5–3 % in elective extremities surgery [3].

POD presents a serious clinical challenge due to its association with adverse outcomes such as prolonged mechanical ventilation, extended stays in intensive care units, increased mortality rates (up to 23 % in hospitalized patients, with a 38 % rise at 6 months in those who experienced delirium) and heightened healthcare costs [9–11]. It is also associated with higher long-term morbidity and mortality, with an increase in the rate of hospital readmission (27 % in patients with delirium vs. 13.8 % without delirium) and an increase in mortality after discharge [8,12]. In addition, POD acts as an independent risk factor for the long-term development of cognitive impairment, decreased physical capacity and decreased quality of life [13]. The etiology of delirium is multifactorial, with modifiable risk factors accounting for approximately 30–40 % of cases in hospitalized patients, thus presenting opportunities for prevention [14]. The challenge associated with its treatment – early identification of modifiable risk factors – allows us to improve its impact on patient outcomes [15,16]. For this reason, prediction models have been developed, such as PRE-DELIRIC (PREdiction of DELIRium in ICu

[1] Equal contribution.

patients) [17] and DELIPRECAS (DELIrium PREvention CArdiac Surgery) [18], aimed at detecting patients at high risk of developing delirium.

There are still few studies evaluating the incidence of delirium and its risk factors in the general surgical population, with most studies focusing on specific surgical procedures [4,5] or populations [19] with limited cohort numbers [11,16,20] and employing varying diagnostic methods [10]. Similarly, it is widely accepted that delirium reaches its highest incidence within the week following surgery, with higher prevalence between the second and third day after surgery, but there is wide variability among studies regarding the ideal time for its detection [21].

With our prospective multicenter study in Spain, the main objective was to establish the incidence of early POD in Spanish hospitals. As secondary objectives, we aimed to determine the incidence of delirium according to the type of surgical intervention, along with the influence of risk factors on its development. Unlike previous studies, our work adopts a comprehensive approach by evaluating preoperative, intraoperative and postoperative risk factors. Additionally, to enhance the novelty of our study, we have incorporated an analysis of the potential benefits of delirium prevention, estimating its impact on reducing hospital stays, healthcare costs, and mortality. Furthermore, we emphasize the inclusion of a broad 60-day follow-up period, which allows us to assess the medium-term consequences of POD and better understand its clinical progression. This extended time horizon, together with our comprehensive risk factor assessment, differentiates our study from previous literature and provides a more complete picture of POD.

2. Material and methods

2.1. Study design

A prospective multicenter study was designed, divided into three phases: (1) recruitment and assessment of patients on two specific days simultaneously in all participating centers; (2) evaluation of their progress at 2 days postoperatively; and (3) evaluation at 60 days, because delirium-related complications such as functional decline and readmissions often extend beyond the first month. Inclusion criteria for the study were: adult patients over 18 years of age undergoing surgical intervention, urgent or scheduled, requiring hospital admission under any type of anesthesia. Patients with a history of preoperative delirium, defined as a documented history of delirium in a previous hospitalization or surgery, and outpatient surgeries were excluded. A total of 68 Spanish hospitals were included in the study, of which 43 were finally eligible for data collection (the remaining 25 hospitals were excluded due to reasons such as lack of approval from institutional review boards, limited research resources, or incomplete data submission) (eTable 1). On 14 and 21 November 2023, all patients were consecutively registered using a specific online clinical report form on the RedCap platform. The study received approval from the Ethics Committees of the University Hospital of Pontevedra, identified by the code PI 2021/479. Additionally, each participating hospital's ethics committee granted approval and all patients provided informed consent for their inclusion in the study. The trial was registered prior to patient enrollment at clinicaltrials.gov (NC-T06127901). The writing of the manuscript was carried out according to the STROBE statement.

2.2. Risk factors and diagnosis of delirium

A literature review was conducted to identify possible risk factors for the development of POD, based on those identified in previous validated studies [16,18]. On the second postoperative day, the development of delirium was evaluated as the primary outcome using the CAM, CAM-ICU and telephone 4AT scales, according to the patient's postoperative situation at that time. The CAM is a well-validated used tool for delirium detection in clinical practice, supported studies such as Inouye et al. [22] which confirmed its reliability and clinical utility across diverse patient populations. The evaluation and diagnosis of delirium were carried out by the responsible physicians of each unit. All physicians at participating hospitals received the same training; they received online modules on the application of diagnostic methods, explanatory videos for consultation, and individualized support throughout the study in order to maintain a correct and uniform application in the evaluation of the development of delirium. (eMethods).

2.3. Statistical analysis

We estimated the sample size to be 2282, assuming the percentage of delirium in the general surgical population is around 3 %, with a precision of 0.7 % and a confidence level of 95 %. The proportion of missing data was low (ranging from 0 % to 2.1 % depending on the variable). A complete-case analysis was performed, excluding missing data from each specific analysis. No imputation methods were applied.

Data were analyzed using software R, version 4.3.2. The Kolmogorov-Smirnov test was used to check for normality. Quantitative variables are presented as the median and interquartile range because they do not follow a normal distribution, whereas qualitative variables are presented according to their frequency distribution. Differences between groups were assessed using the chi-square test for categorical variables and the Mann-Whitney *U* test for continuous variables. Fisher's exact test was applied when the expected frequency in any cell was less than 5.

A univariate logistic regression was conducted with delirium as the outcome variable (eTable 5). Variables with $p < 0.1$ were selected for further analysis. Two multivariate logistic regressions were performed using these significant variables (eTables 6,7). Collinearity was checked and, if present, variables explaining the same factor were excluded from the same model. One model was focused on preoperative risk factors and the other on intraoperative and postoperative risk factors. To ensure the correct temporal sequence, intraoperative and postoperative variables were only included as risk factors if they were recorded prior to the onset of delirium in each patient. To avoid immortal time bias, survival time was counted from postoperative Day 2 onwards for all patients, regardless of delirium status, since delirium was assessed specifically on Day 2.

Furthermore, Cox regression was conducted, with mortality at 60 days as the outcome variable and age, American Society of Anesthesiologists (ASA) classification and delirium as risk factors. Finally, the probability of death to Day 60 after delirium was analyzed using Kaplan-Meier curves and tested with the log-rank test; two-sided $p < 0.05$ was considered statistically significant.

3. Results

During the study period, a total of 2442 surgical patients were registered. The incidence of delirium in this population was 3.93 % ($n = 96$), with the hyperactive type being the most prevalent, comprising 65.6 % of all delirium cases, followed by the hypoactive type at 34.4 % (eTable 2). The most used drugs in its treatment were haloperidol (54.2 %), dexmedetomidine (8.3 %) and others (37.5 %) (eTable 3).

Table 1 describes the preoperative characteristics of patients with and without delirium. There were no statistically significant differences between genders in either group. The average age in the delirium group was 76 ± 16 years. Taking this into consideration, an analysis of delirium incidence was conducted according to age range, resulting in an increase of up to 7 % incidence in patients over 78 years old (eFigure 1). Likewise, patients who developed delirium obtained significantly higher scores on the Short Blessed Test (SBT) compared to patients who did not develop delirium (10 ± 14 vs. 2 ± 6; $p < 0.001$). A lower educational level, the patient's residence being an institution rather than their personal home and the presence of hearing deficits (hearing loss and use of hearing aids) had a statistically significant association

Table 1
Preoperative characteristics of patients with and without postoperative delirium.

	No Delirium (*n* = 2346)	Delirium (n = 96)	*p*-value
Age, median (IQR), y	63 (50–73)	76 (67–85)	<0.001
Gender, No. (%)			
Male	1219 (51.9)	47 (49.0)	
Female	1127 (48.0)	49 (51.0)	0.564
Residence, No. (%)			
Non-institutionalized	2319 (98.8)	82 (85.4)	<0.001
Institutionalized	27 (1.15)	14 (14.6)	
Cognitive function, median (IQR), (Short Blessed Test)	2 (0–6)	10 (4–18)	<0.001
Morbidities, No. (%)			
Smoker	458 (19.5)	15 (15.6)	0.344
Substance use disorder (SUD)	56 (2.4)	3 (3.1)	0.903
Alcoholism	1223 (52.1)	59 (61.5)	0.073
Anxious-depressive disorders	493 (21.0)	24 (25)	0.349
Diabetes mellitus	483 (20.6)	24 (25)	1.000
Parkinson	22 (0.9)	5 (5.2)	0.003
Cerebrovascular disease	134 (5.7)	12 (12.5)	0.006
Hypertension	1018 (43.4)	64 (66.7)	<0.001
Coronary artery disease	171 (7.3)	11 (11.5)	0.185
Valvular heart disease	113 (4.8)	9 (9.4)	0.076
Peripheral vascular disease	143 (6.1)	11 (11.5)	0.054
Respiratory disease	150 (6.4)	4 (4.2)	0.505
Renal failure on dialysis	31 (1.3)	2 (2.1)	0.855
Serum sodium levels (mEq/L) median (IQR)	140 (138–142)	139 (137–141)	0.001
ASA Physical Status Classification System, No. (%)			
I	277 (11.8)	3 (3.12)	<0.001
II	1293 (55.2)	34 (35.4)	
III	701 (29.9)	53 (55.2)	
IV	69 (2.95)	6 (6.25)	
Educational level, No. (%)			
No formal education	138 (5.9)	15 (16.0)	
Elementary education	768 (33.3)	43 (45.7)	
High school education	928 (40.2)	25 (26.6)	<0.001
College education	475 (20.6)	11 (11.7)	
Hearing impairment, No. (%)	273 (11.6)	27 (28.1)	<0.001
Visual deficits, No. (%)	922 (39.3)	43 (44.8)	0.331
COVID-19, No. (%)	1283 (54.7)	50 (52.1)	0.691
Medical treatments, No. (%)			
Opioids	235 (10.0)	17 (17.7)	0.015
	No Delirium (n = 2346)	Delirium (n = 96)	p-value
Medical treatments, No. (%)			
Statins	773 (32.9)	39 (40.6)	0.118
Angiotensin-converting enzyme inhibitors	457 (19.5)	26 (27.1)	0.067
Angiotensin receptor blockers	380 (16.2)	24 (25)	0.023
Benzodiazepines	497 (21.2)	30 (31.2)	0.019
Surgical specialties, No. (%)			
Digestive surgery	577 (24.6)	15 (15.6)	<0.001
Urological	321 (13.7)	6 (6.2)	
Gynecological	172 (7.3)	6 (6.2)	
Otorhinolaryngology	128 (5.5)	2 (2.1)	
Maxillofacial	60 (2.6)	5 (5.2)	
Neurosurgery	122 (5.2)	5 (5.2)	
Cardiac	61 (2.6)	7 (7.3)	
Vascular	107 (4.6)	10 (10.4)	
Plastic-reconstructive	74 (3.1)	1 (1.0)	
Orthopedic traumatology	582 (24.8)	35 (36.5)	
Ophthalmologic	8 (0.34)	0 (0)	
Other	134 (5.7)	4 (4.2)	

Data are presented as absolute numbers, percentages, or medians with corresponding 25th and 75th percentiles (interquartile range; IQR), as appropriate. **ASA:** American Society of Anesthesiologist. **COVID-19:** Coronavirus disease. y: years.

Table 2
Intraoperative and postoperative characteristics of patients with and without postoperative delirium at day 2.

	No Delirium (n = 2346)	Delirium (n = 96)	p-Value
Intraoperative			
Type of surgery, No (%)			
Elective surgery	2157 (91.9)	83 (86.5)	0.056
Emergency surgery	189 (8.1)	13 (13.5)	
Type of anesthesia, No (%)			
Inhalatory anesthesia	1183 (50.4)	44 (45.8)	0.437
TIVA	448 (19.1)	22 (22.9)	0.352
Neuroaxial anesthesia	649 (27.7)	33 (34.4)	0.151
Hypnosis monitoring, No (%)	1401 (59.7)	64 (66.7)	0.209
Medical treatments, No (%)			
Neuromuscular blockers	1531 (65.3)	64 (66.7)	0.862
Neuromuscular blockade reversal			
Sugammadex	1268 (54.0)	42 (43.7)	0.007
Neostigmine	47 (2)	7 (7.3)	
No reversal	1031 (43.9)	47 (49.0)	
Ketamine	156 (6.6)	11 (11.5)	0.105
Benzodiacepines	1321 (56.3)	54 (56.2)	1
Opioids	2041 (87)	83 (86.5)	1
Dexmedetomidine	37 (1.6)	0 (0)	0,416
Transfusion, No (%)	72 (3.1)	18 (18.7)	<0.001
Surgical bleeding, median (IQR),mL	100 (30−200)	200 (60–350)	<0.001
Vasoactive drugs, No (%)	450 (19.2)	45 (46.9)	<0.001
Duration of surgery, median (IQR), min	100 (60–155)	120 (75–235)	0.001
Postoperative			
Hospital admission profile, No (%)			
ICU	403 (17.2)	28 (29.2)	0.010
PACU	1700 (72.5)	60 (62.5)	
Another	243 (10.4)	8 (8.3)	
Temperature at admission, median (IQR), °C	36.1 (35.8–36.5)	36 (35.4–36.5)	0.076
Medical treatments, No (%)			
Opioids	1004 (42.8)	53 (55.2)	0.021
Dexmedetomidine	14 (0.6)	5 (5.2)	<0.001
Benzodiacepines	426 (18.2)	34 (35.4)	<0.001
Vasoactive drugs	98 (4.2)	16 (16.7)	<0.001
Postoperative pain at admission, median (IQR), VAS	1 (0–4)	1 (0–3)	0.574
Postoperative pain when CAM/CAM-ICU or 4AT scale is performed, median (IQR), VAS	2 (0–4)	2 (1–5)	0.023
Endotracheal intubation time, median (IQR), d	0 (0–1)	1 (1–4)	<0.001
	No Delirium (n = 2346)	Delirium (n = 96)	p-value
Length of ICU stay, median (IQR), d	1 (0–1)	2 (1–5.5)	<0.001
Length of hospital stay, median (IQR), d	3 (2–6)	7(3–12)	<0.001
Mortality at 60 days, No (%)	15 (0.64)	8 (8.33)	<0.001

Data are presented as absolute numbers, percentages, or medians with corresponding 25th and 75th percentiles (interquartile range; IQR), as appropriate **CAM:** Confusion Assessment Method, **CAM-ICU**: Confusion Assessment Method for the ICU,. **°C**: degrees Celsius, **d**: days, **ICU**: Intensive Care Units, **min**: minutes, **ml:** milliliter**, PACU:** Post-Anesthesia Care Unit, **VAS**: Visual analog scale.

with the development of POD, as well as previous treatment with benzodiazepines. Analyzing incidence by surgical type revealed that the highest percentage of delirium cases occurred after orthopedic traumatology procedures (36.5 %), followed by digestive (15.6 %), vascular (10.4 %), and cardiac (7.3 %) surgery.

Table 2 describes the intraoperative and postoperative characteristics of patients with and without delirium. Intraoperatively, regarding possible risk factors associated with delirium, a statistically significant relationship was found between the increased surgical bleeding (200 mL vs. 100 mL; $p < 0.001$), the need for blood transfusion (18.7 % vs. 3.1 %; $p < 0.001$) and the use of vasoactive drugs (46.9 % vs. 19.2 %; $p < 0.001$). During the postoperative period, patients who developed delirium were characterized by higher length of hospital stay (7 days vs. 3 days; $p < 0.001$) and ICU stay (2 days vs. 1 day; $p < 0.001$), as well as a greater need for treatment with vasoactive drugs (16.7 % vs. 4.2 %; $p < 0.001$).

No significant differences in hemodynamic values were found between both groups (eTable 4).

These results were transferred to an age- and gender-adjusted univariate analysis (eTable 5) and those variables with $p < 0.1$ were included in a backward stepwise multivariate analysis, resulting in four independent preoperative risk factors for the development of delirium: patient age (odds ratio [OR] = 1.06, 95 % confidence interval [CI] = 1.03–1.08; $p > 0.001$), SBT score > 6 points (OR = 1.12, 95 % CI = 1.08–1.15; $p < 0.001$), substance use disorder (SUD) (OR = 3.97, 95 % CI = 1.05–14.93; $p = 0.042$) and alcoholism (OR = 1.92, 95 % CI = 1.20–3.07; $p = 0.006$) (Fig. 1A and Table 3).

Similarly, at the intraoperative level, blood transfusion (OR = 3.31,

Table 3
Multivariate analysis to assess the risk of delirium onset, focusing on preoperative risk factors.

	OR	95 % CI	p-value
Age (years)	1.055	(1.035, 1.076)	<0.001
Cognitive function (SBT)	1.113	(1.081, 1.147)	<0.001
Drug abuse	3.745	(1.011, 13.875)	0.048
Alcoholism	1.907	(1.211, 3.003)	0.005

OR: Odds ratio, **95 % CI**: 95 % Confidence Interval.

Table 4
Multivariate analysis to assess the risk of delirium onset, focusing on intraoperative and postoperative risk factors.

	OR	95 % CI	p-value
Age (years)	1.071	(1.051, 1.092)	<0.001
Transfusion	3.256	(1.725, 6.147)	<0.001
Postoperative pain	1.111	(1.019, 1.210)	0.017
Vasoactive drugs	2.170	(1.377, 3.421)	0.001

OR: Odds ratio, **95 % CI**: 95 % Confidence Interval.

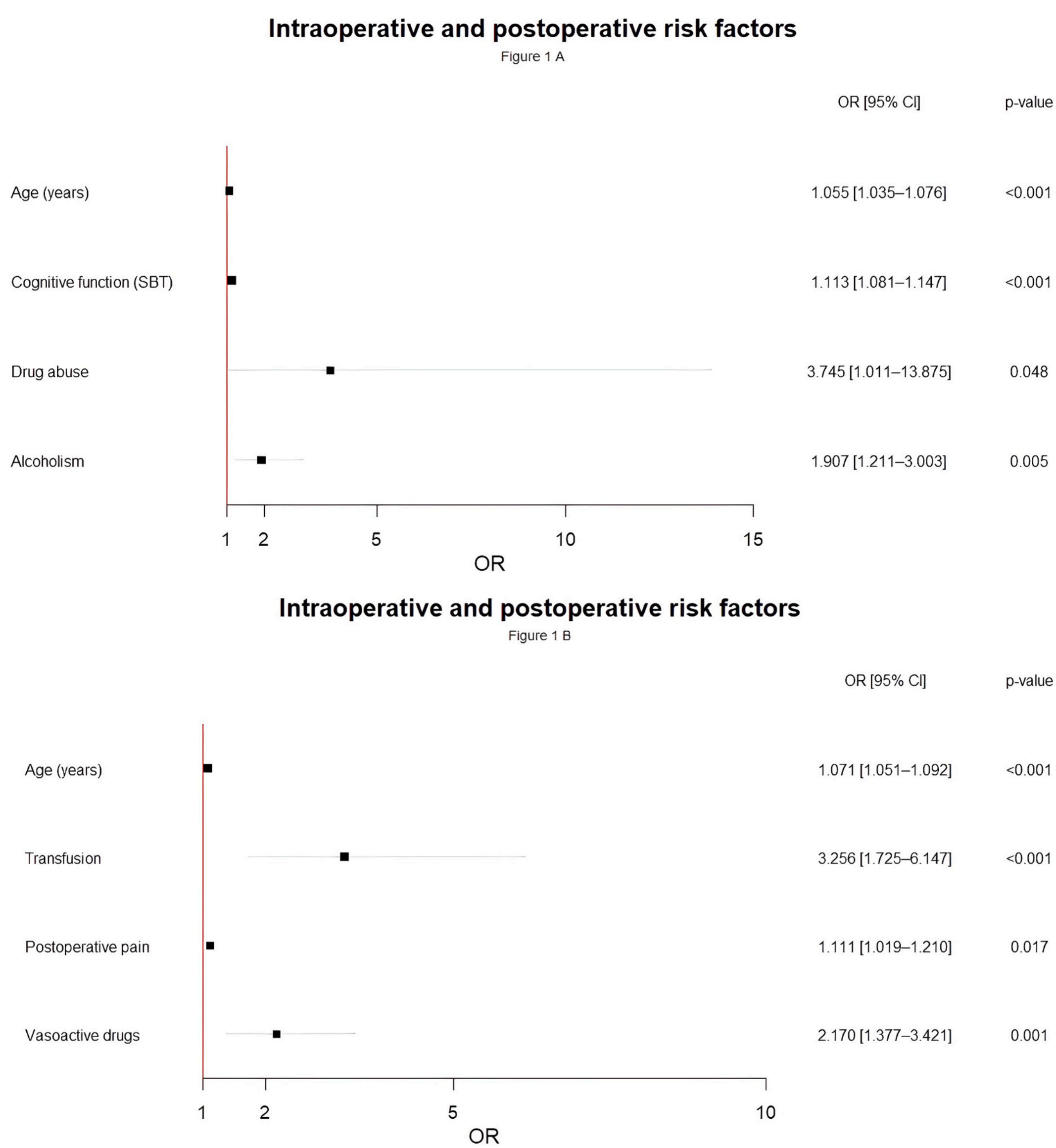

Fig. 1. Multivariate analysis to assess the risk of delirium onset, distinguishing between preoperative (1A) and intra/postoperative (1B) factors.

95 % CI = 1.73–6.36; $p > 0.001$) was identified as an independent risk factor in the multivariate analysis for the development of delirium, and at 48 h post-surgery, postoperative pain (OR = 1.09, 95 % CI = 1.02–1.16; $p = 0.012$) and the need for vasoactive drugs (OR = 2.69, 95 % CI = 1.41–5.15; $p = 0.003$) were also identified as risk factors (Fig. 1B and Table 4).

On average, Kaplan-Meier survival curves for 60-day mortality in patients who developed delirium indicate that they died earlier (log-rank $p < 0.0001$) (Fig. 2).

In the Cox multivariate analysis (Fig. 3 and Table 5), delirium at Day 2 was independently associated with 60-day mortality (HR = 4.07, 95 % CI = 1.53–10.83; $p = 0.005$), as well as age (HR = 1.07, 95 % CI = 1.03–1.12; $p = 0.002$) and ASA classification (HR = 2.49, 95 % CI = 1.25–4.94; $p = 0.009$).

4. Discussion

To our knowledge, this is the first national multisite prospective study with a large population-based cohort to evaluate surgical patients for POD using validated assessments. We found that: the incidence of POD was 3.93 %; orthopedic surgery carries the highest risk of delirium (36.5 %), followed by digestive (15.6 %) vascular (10.4 %) and cardiac (7.3 %) surgery; preoperative risk factors include advanced age, cognitive function deterioration (SBT > 6), SUD and alcoholism, whereas in the intraoperative and postoperative period (Day 2) the risk factors include blood transfusions, postoperative pain and vasoactive treatment; and patients with delirium are associated with worse postoperative outcomes, such as longer hospital stays, with increased mortality at Day 60.

4.1. Incidence of postoperative delirium

POD rates range from 1.9 % [23] in a recent retrospective study in New Zealand to 3 % in a review by Jin et al. [3]. Hernández et al. [21] in their systematic review on POD, showed that the evidence remains variable and proposed that a large cohort study is required to clarify the different facets of postoperative cognitive abnormalities. Our study, with a 3.93 % incidence, aligns with previous findings.

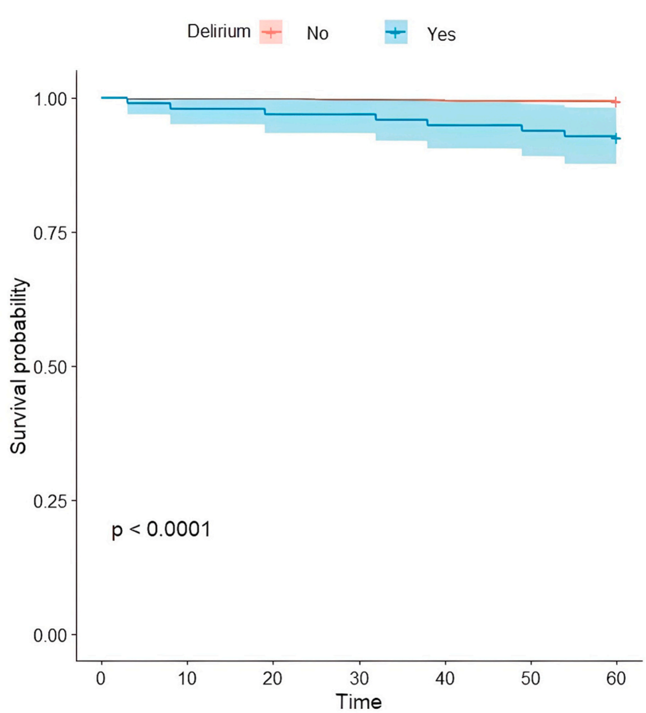

Fig. 2. Kaplan-Meier survival curves for 60-day mortality.

The incidence of delirium increases with age. In a study across five hospitals in England the incidence was 6.5 % among adults aged 65 years or older undergoing major surgery [24]. These results are similar to those obtained in our study, where the age-adjusted incidence of delirium in patients over 78 years of age showed an increase in the incidence of POD up to 7 %.

The incidence of POD varies depending on the type of surgical intervention performed; for example, in trauma surgeries, factors such as femur fractures in frail elderly patients, perioperative pain and emergency settings contribute to the higher incidence of delirium [3]. In our study, the highest percentage of POD was in orthopedic traumatology surgery (36.5 %), followed by digestive (15.6 %), vascular (10.4 %) and cardiac (7.3 %) surgery. Ophthalmological surgery had the lowest rate, with no recorded cases of delirium. In the case of cardiac surgery, the incidence of delirium was 7.3 %, which is lower than reported in previous studies [18]. This could be attributed to the increased focus on delirium prevention measures in critical care units, in which, with historically higher rates, greater emphasis is currently placed on its control and prevention [17].

4.2. Risk factors

A recent Cochrane review found that multicomponent interventions effectively prevent delirium in hospitalized patients, emphasizing the need to address risk factors for better prevention [25]. As recommended in previous research [26], we derived the risk factors used in our study from a systematic review of the literature. Advanced age is a widely recognized and established risk factor for delirium development, as supported by a recent meta-analysis on perioperative factors [27], and is also included in validated scales for early detection [18,21]. Our study not only validates the association between age and increased risk of delirium but also demonstrates that the incidence of delirium nearly doubles in the surgical population over 78 years old. This current systematic review and meta-analysis [27] further supports previous research findings on the presence of preoperative cognitive impairment as a risk for POD [18,25,28], which was assessed in our study using the SBT; a cutoff point of >6 points on the SBT was identified. Likewise, SUD and excessive alcohol consumption have been recognized as preoperative factors for delirium [24]. Shah et al. in their study, which aimed to determine the relationship between alcohol consumption and the risk of developing POD, found as risk factors: alcohol-related laboratory test (mean red blood cell volume > 95.0 femtoliters), having ever received advice to reduce alcohol consumption and not abstaining from drinking alcohol for at least one continuous week in the previous year. They also found as risk factors related to POD advanced age and preexisting cognitive impairment [29].

Our study identified intraoperative blood transfusion as a risk factor for POD. This finding aligns with several large observational studies. A recent systematic review [30] confirm this association, and earlier studies, like Krych et al. [31] with 8792 cardiac surgery patients, and Gao et al. [32] with 549 spinal surgery patients, also support this link. In relation to this, our study also identified an association between surgical bleeding and the risk of POD, which has been reported previously in studies such as that of An et al. [33], who observed a higher risk of delirium with increased surgical bleeding in patients undergoing hip fracture surgery. Similarly, Olin et al. [34] and Marcantonio et al. [35] found that patients who developed POD had significantly higher intraoperative blood loss, received more intravenous fluid and needed more blood transfusions than those who did not develop POD. Our current findings support and corroborate these previous research results.

Regarding postoperative outcomes, inadequate treated pain is a well-known precipitating factor for the development of POD [36,37]. In a study involving 541 patients undergoing hip surgery, it was found that those with untreated pain were nine times more likely to develop delirium compared to those who received adequate analgesic treatment

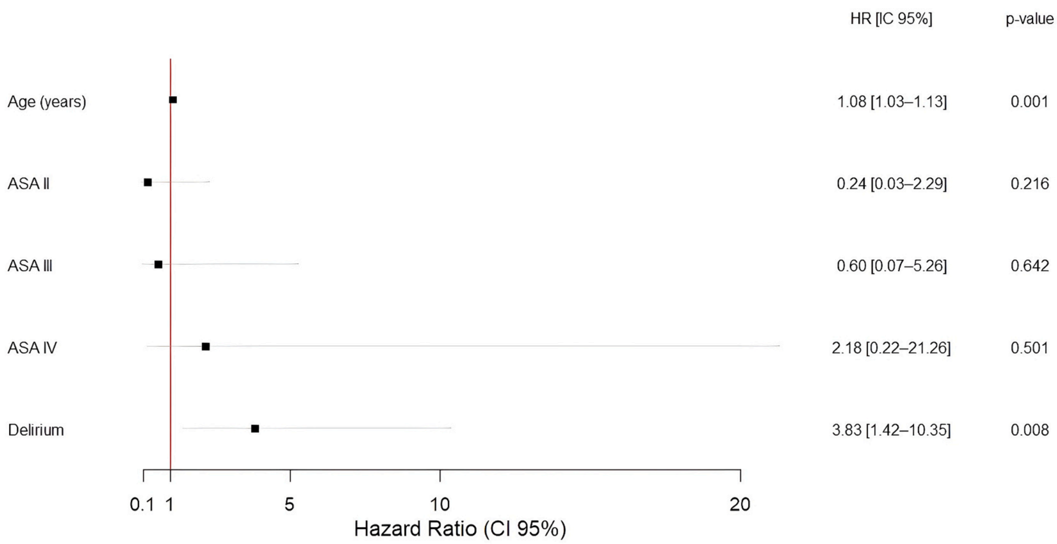

Fig. 3. Estimates of the effect of covariates on mortality in Cox proportional hazards models.

Table 5
Estimates of the effect of covariates on mortality in Cox proportional hazards models.

		HR	95 % IC	p-value
Age		1.079	(1.032, 1.127)	0.001
ASA	I (Ref)			
	II	0.243	(0.026, 2.289)	0.216
	III	0.597	(0.068, 5.256)	0.642
	IV	2.184	(0.224, 21.262)	0.501
Delirium		3.828	(1.416, 10.348)	0.008

HR: Hazard ratio, **95 % CI:** 95 % Confidence Interval, **ASA**: American Society of Anesthesiologist physical status classification, **Ref**: reference category.

[37]. These findings are further supported by a recent meta-analysis that showed a lower incidence of delirium following implementation of the ABCDEF package, which includes measures to "Assess, Prevent and Manage Pain" [38]. Additionally, our research identifies the use of vasoactive drugs as a risk factor for POD in the postoperative period. The use of these drugs in the context of hemodynamic instability or prolonged hypotension in patients has been established previously as a contributing factor [39].

4.3. Long-term outcomes

Delirium is a serious complication with significant short- and long-term consequences. Supported by a recent Cochrane review [25] and preceding research, delirium is recognized as an important prognostic factor [40], as in the meta-analysis of nearly 3000 references that showed that delirium is associated with a higher risk of death compared to controls after an average follow-up period of 22.7 months [41]. Our findings indicate that POD is an independent risk factor for increased 60-day mortality in postsurgical patients (8.2 % vs. 0.9 %; $p < 0.001$).

Likewise, delirium is associated with poorer outcomes, including an increased length of hospital stay [40,42]. In our study, the average length of stay was also found to be more than double in patients who experienced delirium compared to those who did not.

4.4. Clinical relevance and applicability

In Spain, in the year 2022, a total of 3,534,800 surgical procedures were performed [43]. Assuming a delirium incidence of 4 % based on our study, 140,006 individuals would develop delirium. According to our findings, patients with delirium have an in-hospital mortality rate of 8.2 %, compared to 2 % in those without delirium. Applying this excess mortality (6.2 %) to the 140,006 affected individuals results in an estimated 8680 potentially avoidable deaths. If we consider the total mortality among patients with delirium (8.2 %), this figure rises to 11,480 potentially preventable deaths. It is important to note that these estimates are not directly derived from our cohort, but represent a theoretical extrapolation to the national surgical population in Spain. We used the total number of surgical procedures reported in Spain in 2022 (reference 43) and applied the incidence and mortality rates observed in our study to illustrate the potential public health impact of postoperative delirium. This approach aims to contextualize our findings and highlight the broader implications of delirium prevention and management.

Preventive measures could significantly reduce the burden of delirium in surgical patients. Evidence suggests that such strategies may decrease delirium incidence by 30 % to 50 %, preventing 42,000 to 70,000 cases annually [22], and shorten hospital stays by 1.5 to 3 days per patient, leading to 210,000 to 420,000 fewer hospital days [44]. With an estimated daily hospital cost of 800 to 1200 euros, this reduction could yield annual savings of 168–504 million euros. Additionally, since delirium has an 8.2 % mortality rate, these measures could prevent 3444 to 5740 deaths per year [45]. Given these significant implications, evaluating patients one year post-surgery remains essential to assess their quality of life and mortality. Implementing evidence-based strategies—such as optimized pain management, early mobilization, cognitive reorientation, and sleep optimization—could improve both patient outcomes and healthcare system efficiency [41,46].

4.5. Limitations

Our study had several limitations. Firstly, we did not assess potential preventive measures or factors that could influence the perioperative period and its impact on the development of delirium. These factors may vary among the different hospitals participating in the study. As our aim was to evaluate the current situation in Spain, we did not include these variables. Secondly, evaluating delirium only at a single time point two days after surgery may have led to an underestimation of its incidence, as cases developing later would have been missed. However, considering the size of the hospitals and the large number of patients involved, along with previous methodologies indicating that POD peaks around postoperative Day 2–3 [3,47], we believe that this cut-off point was appropriate for achieving our study objectives. To improve our understanding of delirium in this group of patients, future studies should focus on comparable risk factors and methods of data collection, as well as possible collaborative work.

5. Conclusions

This large multicenter prospective observational study of surgical patients, involving 43 Spanish hospitals and over 2400 patients, has provided valuable insights into the current national incidence of POD. Additionally, we have identified preoperative and intra- and post-operative risk factors associated with the development of delirium. Our study also highlights delirium as a risk factor for poor postoperative outcomes, including prolonged hospital stay and increased mortality 60-days post-surgery. These findings underscore the importance of early detection and targeted treatment of POD. Early identification of high-risk patients plays a critical role in preventive measures, reducing adverse events and improving outcomes in healthcare settings. Moreover, the data generated in this study can be extrapolated to estimate the nationwide burden of postoperative delirium in Spain, quantifying its impact on healthcare cost, hospital length of stay and mortality rates. This can help policy decisions and resource allocation aimed at delirium prevention and management.

CRediT authorship contribution statement

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Author statement

All authors have accepted responsibility for the entire content of this manuscript and consented to its submission to the journal, reviewed all the results and approved the final version of the manuscript.

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Declaration of competing interest

- The work described has not been published previously.
- The article is not under consideration for publication elsewhere.
- The article's publication is approved by all authors.
- If accepted, the article will not be published elsewhere in the same form, in English or in any other language, including electronically, without the written consent of the copyright-holder.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinane.2025.112018.

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