Aging Clinical and Experimental Research
https://doi.org/10.1007/s40520-022-02099-8

ORIGINAL ARTICLE

Prevalence and features of delirium in older patients admitted to rehabilitation facilities: a multicenter study

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Received: 17 January 2022 / Accepted: 16 February 2022

Abstract

Background Delirium is thought to be common across various settings of care; however, still little research has been conducted in rehabilitation.

Aim We investigated the prevalence of delirium, its features and motor subtypes in older patients admitted to rehabilitation facilities during the three editions of the "Delirium Day project".

Methods We conducted a cross-sectional study in which 1237 older patients (age ≥ 65 years old) admitted to 50 Italian rehabilitation wards during the three editions of the "Delirium Day project" (2015 to 2017) were included. Delirium was evaluated through the 4AT and its motor subtype with the Delirium Motor Subtype Scale.

Results Delirium was detected in 226 patients (18%), and the most recurrent motor subtype was mixed (37%), followed by hypoactive (26%), hyperactive (21%) and non-motor one (16%).

In a multivariate Poisson regression model with robust variance, factors associated with delirium were: disability in basic (PR 1.48, 95%CI: 1.17–1.9, *p* value 0.001) and instrumental activities of daily living (PR 1.58, 95%CI: 1.08–2.32, *p* value 0.018), dementia (PR 2.10, 95%CI: 1.62–2.73, *p* value < 0.0001), typical antipsychotics (PR 1.47, 95%CI: 1.10–1.95, *p* value 0.008), antidepressants other than selective serotonin reuptake inhibitors (PR 1.3, 95%CI: 1.02–1.66, *p* value 0.035), and physical restraints (PR 2.37, 95%CI: 1.68–3.36, *p* value < 0.0001).

Conclusion This multicenter study reports that 2 out 10 patients admitted to rehabilitations had delirium on the index day. Mixed delirium was the most prevalent subtype. Delirium was associated with unmodifiable (dementia, disability) and modifiable (physical restraints, medications) factors. Identification of these factors should prompt specific interventions aimed to prevent or mitigate delirium.

Keywords Delirium · Rehabilitation · Dementia · Disability · Physical restraint

Background

Delirium, as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), is an acute neuropsychiatric syndrome with disturbance in attention and cognitive functions and fluctuation over the course of hours or days [1]. It is associated with several negative events, including increased mortality in the middle–long term, prolonged hospitalization with elevated healthcare costs, and progression of cognitive and functional decline, especially in patients with pre-existing dementia [2–4].

Delirium is known to be common across various settings of care [5]. However, while consistent data regarding delirium prevalence and incidence are available for specific settings, i.e., acute hospital wards and intensive care units, few research has been conducted in the rehabilitative settings, the few exceptions consisting of analyses based on small number (1 to 3) of rehabilitation units [6–8]. This means that

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Published online: 08 April 2022

a lack of important information exists regarding the prevalence of delirium in these settings.

To fill this gap, we used the database of the Delirium Day project (DD), an initiative to improve the awareness of delirium across healthcare operators in Italy. The DD initiative conducted one multicenter study along three consecutive years (2015, 2016 and 2017), involving not only acute hospital but also rehabilitation wards.

The aim of this study is to assess the prevalence of delirium and its psychomotor subtypes among older patients admitted to a large number of rehabilitation wards in Italy. A second aim is to detect patients' features associated with delirium, to support possible interventions in these settings.

Methods

Participants

In this cross-sectional study, we included older inpatients admitted to 50 Rehabilitation facilities collected during the DD studies from 2015 to 2017.

As discussed in detail in related articles, the eligible criteria for inclusion of the patients were (i) age ≥ 65 years old (ii) native Italian speakers and (iii) a subscription of informed consent; exclusion criteria, on the other hand, was refusal or inability to consent [9–13].

Data collection

All patients were screened for the presence of delirium by the attending physician on each site using the 4AT, a scale validated for delirium; we considered the presence of delirium if the patient obtained a score equal or greater than 4 upon a total of 12 points [14, 15]. Moreover, patients with delirium were assessed with the Delirium motor subtype scale (DMSS) for the related motor subtype (hyperactive, hypoactive, mixed and no-motor delirium) [16].

The data collected also included sociodemographic (sex, age) and clinical status (Charlson Comorbidity Index), total amount and type of medications prescribed, presence of in situ medical devices (peripheral venous catheter and urinary catheter) and physical restraints [17].

A variable named "Disability in basic activities" evaluating the autonomy in the basic activities of daily living (BADLs) [18] was created by assessing the patient's capability to self-feeding, self-dressing and self-transferring. "Autonomy/partial disability" was recorded if the patient was able to perform each task independently or if the patient was unable to perform one or two activities without assistance; "disability" if the patient needed help performing all three tasks. A second variable named "Disability in instrumental activities" was created addressing the ability in in the instrumental activities of daily living (IADLs) [19], including shopping and managing their own medications. The inclusion of only three BADLs and two IADLs was related to the study protocol and the data collection limited to these items in the three consecutive years. We have decided to collect three specific BADLs, which would provide the functional autonomy of the patients, and two major IADLs which are more complex and also indicative of a possible underline dementia and frailty.

Dementia data were recorded as present if it was documented in the medical chart, and/or the patient was receiving acetylcholinesterase inhibitors or memantine.

The study protocol for Delirium day events was approved from the Ethical Committees of the IRCCS Fondazione Santa Lucia, Rome (year 2015) and of the University of Milano–Bicocca, Monza, Italy (years 2016–2017).

Statistical analysis

Demographic and clinical characteristics were reported for the whole sample and according to delirium status, as percentage for nominal and categorical variables and as median and interquartile range (IQR) for continuous ones. To compare the characteristics between patients with and without delirium, we applied the Chi-square test (or the Fisher test when appropriate) for categorical variables and the Wilcoxon test for continuous variables. The statistical significant was included in a multivariate Poisson regression model with robust variance, able to take into account the problem due to a frequent outcome. The association estimates from the multivariate model were reported as prevalence ratio and corresponding 95% confidence intervals. All hypothesis tests were two-sided and a $p < 0.05$ was considered as significant. To verify the influence of partial functional measurements (BADLs and IADLs) on findings, we performed an additional sensitivity analysis without these variables.

Analyses have been carried out using SAS software, version 9.4 (SAS Institute Inc., Cary, NC).

Results

A total of 1237 inpatients assessed in rehabilitation facilities during the three years of DD events were eligible. Of these 226 patients (18%) had delirium. The demographic, functional, and clinical characteristics of all the subjects, and separately for presence and absence of delirium are displayed in Table 1. The median age of the whole sample was 82 years old and 62.3% were female; around 39% suffered from cerebrovascular disease and 23% from dementia. The use of antidepressants other than SSRI, including trazodone, was 16.3%, typical antipsychotic 7.4% and atypical 9.4%. On the index day, 20% of patients received antibiotics, 26.5%

Table 1 Demographic, and clinical characteristics of 1237 patients in the whole sample and according to the presence of delirium

	Whole sample ($n=1237$)	Delirium ($n=226$)	No delirium ($n=1011$)	P value
Demographic variables				
Age (years), median, (IQR)	82 (76–87)	84 (78–89)	81 (75–87)	<0.0001[‖]
Gender female, *n* (%)	771 (62.3)	119 (52.7)	652 (64.5)	0.0009
Disability*				
In basic activities, *n* (%)	225 (18.2)	97 (42.9)	128 (12.7)	<0.0001
In instrumental activities, *n* (%)	668 (54.4)	187 (83.5)	481 (47.9)	<0.0001
Clinical status				
Dementia (medical chart), *n* (%)	282 (22.8)	122 (54.0)	160 (15.8)	<0.0001
Charlson comorbidity index, median (IQR) [†]	2 (1–4)	3 (2–5)	2 (1–4)	<0.0001
Myocardial infarction, *n* (%)	169 (13.7)	26 (11.5)	143 (14.1)	0.2962
Congestive heart failure, *n* (%)	262 (21.2)	66 (29.2)	196 (19.4)	0.0011
Peripheral vascular disease, *n* (%)	251 (20.3)	47 (20.8)	204 (20.2)	0.8345
Cerebrovascular disease, *n* (%)	476 (38.5)	126 (55.8)	350 (34.6)	<0.0001
Solid tumor, *n* (%)	132 (10.7)	23 (10.2)	109 (10.8)	0.7902
Metastatic solid tumor, *n* (%)	40 (3.2)	6 (2.7)	34 (3.4)	0.5864
Diabetes, uncomplicated, *n* (%)	176 (14.2)	28 (12.4)	148 (14.6)	0.3815
Diabetes, complicated, *n* (%)	101 (8.2)	19 (8.4)	82 (8.1)	0.8831
Chronic pulmonary disease, *n* (%)	213 (17.2)	39 (17.3)	174 (17.2)	0.9868
Hemiplegia, *n* (%)	136 (11.0)	32 (14.2)	104 (10.3)	0.0925
Peptic ulcer disease, *n* (%)	45 (3.6)	7 (3.1)	38 (3.8)	0.6312
Mild liver disease, *n* (%)	54 (4.4)	7 (3.1)	47 (4.7)	0.3021
Moderate-severe liver disease, *n* (%)	34 (2.8)	4 (1.8)	30 (3.0)	0.3195
Renal disease, *n* (%)	167 (13.5)	37 (16.4)	130 (12.9)	0.1624
Rheumatologic disease, *n* (%)	49 (4.0)	6 (2.7)	43 (4.3)	0.2654
Leukemia, *n* (%)	20 (1.6)	3 (1.3)	17 (1.7)	1.0000[§]
Lymphoma,*n* (%)	15 (1.2)	4 (1.8)	11 (1.1)	0.3971[§]
HIV/AIDS, *n* (%)	3 (0.2)	1 (0.4)	2 (0.2)	0.4990[§]
Pharmacological treatment				
Number of drugs, median (IQR)	7 (5–9)	7 (5–9)	7 (5–9)	0.3907 [‖]
Antibiotics, *n* (%)	249 (20.1)	76 (33.6)	173 (17.1)	<0.0001
Steroids, *n* (%)	151 (12.2)	40 (17.7)	111 (11.0)	0.0053
Antidepressants SSRI, *n* (%) [‡]	183 (14.8)	32 (14.2)	151 (15.0)	0.7621
Antidepressants others, *n* (%)	202 (16.3)	58 (25.7)	144 (14.2)	<0.0001
Antipsychotics, typical, *n* (%)	91 (7.4)	43 (19.0)	48 (4.8)	<0.0001
Antipsychotics, atypical, *n* (%)	116 (9.4)	42 (18.6)	74 (7.3)	<0.0001
Benzodiazepines, *n* (%)	376 (30.4)	55 (24.3)	321 (31.8)	0.0285
Anti-epileptics, *n* (%)	102 (8.3)	28 (12.4)	74 (7.3)	0.0122
AChE-I/memantine, *n* (%)	34 (2.8)	7 (3.1)	27 (2.7)	0.7228
Other psychoactive drugs, *n* (%)	70 (5.7)	11 (4.9)	59 (5.8)	0.5689
Medical devices				
Venous catheter, *n* (%)	328 (26.5)	99 (43.8)	229 (22.7)	<0.0001
Urinary catheter, *n* (%)	234 (18.9)	85 (37.6)	149 (14.7)	<0.0001
Physical restraints, *n* (%)	580 (46.9)	182 (80.5)	398 (39.4)	<0.0001

IQR interquartile ranges, *HIV* Human Immunodeficiency Virus, *AIDS* Acquired Immunodeficiency Syndrome, *SSRI* selective serotonin reuptake inhibitors, *AChE-I* acetylcholinesterase inhibitors

[*]Disability in basic activities was defined if the patient was unable to self-feeding, self-dressing and self-transferring. The disability in instrumental activities was defined if the patient needed help in shopping and managing their own medications

[†] 9 missing data; [‡] 1 missing data**;** [§] Fisher exact test; [‖] Kruskal–Wallis test

had peripheral venous catheter in situ and 18.9% had urinary catheter. Almost 47% of them were physically restrained.

Patients with delirium were slightly older (84 vs 81 years), with a lower prevalence of females (52.7% vs. 64.5%) and with a worse functional status (42.9% vs 12.7% for disability in basic activities, and 83.5% vs 47.9% for disability in instrumental activities) than inpatients without delirium. Furthermore, they had a worse clinical profile. In particular, we found a higher prevalence of congestive heart failure (29.2% vs 19.4%), cerebrovascular disease (55.8% vs 34.6%) and dementia (54% vs 15.8%). In addition, they were receiving more antidepressants other than selective serotonin reuptake inhibitors (SSRI) (25.7% vs 14.2%), typical antipsychotics (19% vs 4.8%), atypical antipsychotics (18.6% vs 7.3%), anti-epileptics (12.4% vs 7.3%), as well as more antibiotics (33.6% vs 17.1%) and steroids (17.7% vs 11%) than patients without delirium. The uses of medical devices as venous catheter, urinary catheter and physical restraints were more frequent in patients with delirium.

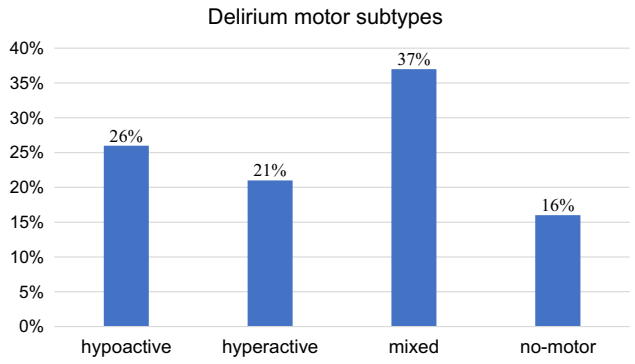

Fig.1 Prevalence of delirium motor subtypes in 200 inpatients during the "Delirium Day"

Figure 1 shows the distribution of the DMSS score which was available only for 200/226 patients with delirium. The most common psychomotor subtype was mixed delirium (37%), followed by hypoactive (26%) and hyperactive delirium (21%); non-motor subtype was manifested only in 16% of inpatient.

The results of the multivariate Poisson regression model with robust variance are reported in Table 2, showing a positive association between delirium and disability in basic (PR 1.48, 95% CI: 1.17–1.9, *p* value 0.001) and instrumental activities (PR 1.58, 95% CI: 1.08–2.32, *p* value 0.018), dementia (PR 2.10, 95% CI: 1.62–2.73, *p* value < 0.0001), typical antipsychotics (PR 1.47, 95% CI: 1.10–1.95, *p* value 0.008), antidepressants other than SSRI (PR 1.3, 95% CI: 1.02–1.66, *p* value 0.035), and physical restraints (PR 2.37, 95% CI: 1.68–3.36, *p* value < 0.0001). To strengthen our results, we performed a separate sensitivity analysis excluding the disability in the basic and instrumental activities in the multivariate Poisson regression model with robust variance, and we did not find evidence for effect modification on positive association between delirium and all above mentioned results (Appendix 1).

Table 2 Prevalence ratio and corresponding 95% confidence intervals (95% CI) from a multivariate Poisson regression. Delirium day 2015, 2016, 2017

Variables	Prevalence ratio	95% Confidence Interval	*P* value
Age	1.00	0.99–1.02	0.665
Gender	0.84	0.67–1.05	0.122
Disability in basic activities	1.48	1.17–1.9	0.001
Disability in instrumental activities	1.58	1.08–2.32	0.018
Dementia	2.10	1.62–2.73	< 0.0001
Congestive heart failure	1.18	0.93–1.51	0.177
Cerebrovascular disease	1.21	0.97–1.52	0.088
Antipsychotics, typical	1.47	1.10–1.95	0.008
Antipsychotics, atypical	1.02	0.77–1.36	0.874
Antidepressants others[a]	1.30	1.02–1.66	0.035
Anti-epileptics	1.22	0.90–1.66	0.189
Benzodiazepines	0.99	0.77–1.29	0.965
Antibiotics	1.08	0.86–1.37	0.487
Steroids	1.19	0.90–1.58	0.217
Venous catheter	1.26	0.99–1.59	0.056
Urinary catheter	1.24	0.97–1.57	0.084
Physical restraint	2.37	1.68–3.36	< 0.0001

[a]Antidepressants other than selective serotonin reuptake inhibitors, including trazodone

Discussion

This multicenter cross-sectional study shows that delirium prevalence in inpatient rehabilitation facilities (IRFs) was 18%, with the mixed delirium subtype being the most common, followed by hypoactive and hyperactive subtypes.

Factors associated with delirium were a pre-existing disability in basic and instrumental activities, dementia, the use of typical antipsychotics and antidepressants other than SSRI along with peripheral venous catheter and physical restraints.

Despite the paucity of studies evaluating delirium in older patients admitted to rehabilitation units, our findings are in line with the existing literature, showing a prevalence of delirium in IRFs from 9.1% to 33% [7, 8, 20–25]. According to a recent review, the prevalence of delirium in IRF is the highest among patients with hip fracture, with coma after trauma or post-stroke [7, 21, 23, 24]. There is however, heterogeneity among studies in the choice of tools for detecting delirium and population samples. In depth, four studies used the Confusion Assessment Method [7, 23–25], one study used the gold standard DSM-5 diagnostic criteria for delirium [22], one chose the Memorial Delirium Assessment Scale [20], and another one the three-minute diagnostic interview for confusion assessment method [8]. None, except our study, used the 4AT. Furthermore, the total number of patients included into these studies ranged from 95 to 1864 inpatients, but cases were derived from a single IRF, except in one study who collected data from four different rehabilitative units [7]. Therefore, the current study adds knowledge in this field by analyzing data obtained from 50 different IRFs.

In our large sample, mixed delirium had the highest prevalence, followed by hypoactive and hyperactive delirium subtypes. Previous studies have shown that the hypoactive subtype is the most common subtype in acute hospital settings; however, very few studies analyzed the prevalence of delirium subtypes selectively in IRFs [9, 26]. In fact, only one research [25] explored the prevalence of delirium psychomotor subtypes in 1864 inpatients in a rehabilitation unit, finding that hypoactive and mixed delirium were the most common, in agreement with our data.

In multivariate analysis, both non-modifiable and modifiable factors were independently associated with delirium. Non-modifiable factors were dementia and pre-existing disability in basic and instrumental activities, while the modifiable factors were the use of typical antipsychotics and antidepressants other than SSRI, along with physical restraints.

Dementia and disability are well-known predisposing factors for the development of delirium [5]. Older patients with dementia are highly prevalent in IRFs, with a delirium prevalence from 8 to 58% [7, 8, 20–25]. Our results confirm the literature, since 22.8% of our patients had dementia and delirium superimposed on dementia (DSD) was observed in more than half of subject with delirium (54%). Similarly, in IRFs studies, patients who developed delirium were found to be more functionally impaired than non-delirious patients, with more adverse outcomes and prolonged hospitalization due to the slow recovery process [23, 24, 26, 27]. This stands for a biological basis, in which both disability and the progressive neurodegeneration of cerebral tissues confer to patients a higher level of basal vulnerability with increased susceptibility to mild stressors [5]. According to the literature, each delirium episode worsens both cognitive [28] and functional status [29] proportionally to its duration, with fivefold increased risk of being institutionalized at discharge and increased mortality after one year [27, 30–32]. Patients who manifested delirium at rehabilitation admission were also considerably at risk to be walking dependent after discharge, and at 1-year follow-up [33].

In our study, dementia and disability in basic and instrumental activities of daily living were associated with a 2.1, 1.48 and 1.58 increased ratio of delirium, respectively, adjusted for covariates. Excluding the disability in the BADLs and IADLs from the multivariate regression model did not modify the positive association between delirium and the other variables.

Cerebrovascular disease and congestive heart failure were also clinical factors independently associated with delirium regardless of patients' functional status. These findings are consistent with the existing literature, in which congestive heart failure is known to be a predisposing factor for delirium in hospitalized patients [34]. Some of the signatures for delirium susceptibility in patients with cardiovascular disease that have been put forward by Correale et al. in their review [34], converge toward (i) elevated sympathetic nerve activities and (ii) autonomic dysregulation leading to cerebral perfusion abnormalities. Moreover, impaired cerebral perfusion is linked to stroke and cognitive impairment that imply cortical and subcortical dysfunctions, accompanied by a reduced cholinergic activity and an increased vulnerability to develop delirium [35, 36]. Monacelli et al. [37] also highlight the correlation between cerebrovascular disease and delirium as a predisposing factor.

Because delirium in hospitalized patients is preventable by mainly acting on precipitating factors [5], we suggest that older people admitted to IRFs should routinely undergo a systematic evaluation of both cognition and functional status soon after admission [38]. This evaluation may be helpful to identify the patients at risk who may be the target for initiatives aimed at avoiding or mitigating delirium.

Modifiable factors for delirium were psychoactive drugs (typical antipsychotics and non-SSRI antidepressants) and the use of physical restraints.

Typical antipsychotics are commonly used by physicians for treating delirium, in particular in presence of patients with severe agitation that potentially may lead to harm themselves or others, despite no clinical benefits have been found in clinical trials and systematic reviews [39]. Hershkovitz and Nissan [40] conducted a retrospective study in a cohort of 448 hip-fractured patient admitted to a rehabilitation unit and found that patients taking antipsychotics lower their functional recovery compared with nonusers. In our study, there was a prevalent use of antipsychotics, which was slightly higher than in Hershkovitz and Nissan's study (16% vs 14%) where an association between them and functional status was drawn. Similarly, in the present work we focused on characterizing the connection between antipsychotics and delirium. In particular, our data seem to suggest an association between the use of antipsychotics and increased risk of delirium, which might worsen patients' functional status. Seeing as how antipsychotics provoke sedation, their prescription could increase the risk of immobilization of the patient, and consequently have a negative effect on functional status and mobility [41]. However, further prospective studies are needed to confirm such findings.

Antidepressants, especially those with anticholinergic property such as tricyclics can induce delirium [42]. In our study, receiving typical antipsychotics on the index day was associated with a 1.47-increased ratio of delirium, while using antidepressants other than SSRI was associated with a 1.3-increased ratio. It is worth stressing, however, that this is a cross-sectional study, that ultimately prevents us to draw definitive causative correlations. Nevertheless, our results point out that physicians working at the IRFs should weight detrimental and beneficial effects of psychoactive drugs and consider their discontinuation whenever possible [43].

The findings about physical restraints also deserve comments. In one study, Nakamizo and colleagues [44] prospectively investigated the incidence of delirium in 387 patients admitted to a Stroke Care Unit with the diagnosis of acute stroke over a nine-month period, finding that the use of physical restraint prior to delirium development resulted to be the most powerful precipitating factor. In our study being physically restrained was associated with a 2.37 increased ratio of delirium, therefore supporting previous findings. The effect of the use of venous and urinary catheters on delirium onset is similar to previous findings from our groups [9, 13].

Implications for the clinical practice are several. Given that, the mixed and hypoactive delirium were the most common subtypes in our study and they usually have the worse prognosis in comparison to hyperactive or no delirium, since their detection are often missed. The systematic screening of delirium presence is therefore recommended for all older patients admitted to rehabilitation facilities. Additionally, factors associated with delirium occurrence must be kept in mind to prevent delirium. In particular, avoiding potentially harmful medications and devices that increase risk of delirium should be promoted. Such approach is recommended in the guidelines of National Institute of Health and Care Excellence (NICE), which hint at the following: (i) remove unnecessary medical devices; (ii) reduce or remove the prescription of psychoactive drugs; (iii) remove physical restraints; (iv) encourage early mobilization and (v) remove environmental barriers [45].

Strengths and limitation of the study

To date, this work is the largest retrospective multicenter nationwide and unique study investigating delirium in rehabilitation settings, including a large sample size with 50 IRFs involved. Another strength is the use of the 4AT test to assess delirium. This tool has been validated among IRFs patients, showing good performance to detect delirium in reference to the DSM criteria [14, 15].

Some limitations should also be mentioned. One limitation is the cross-sectional design of the study, which prevented us to provide information on the temporal and causal direction of the association between delirium and the predisposing and precipitating risk factors. Second, the association between nutritional status and delirium was not evaluated, because of heterogeneity of nutritional data collected in three DD editions. Third, due to the lack of completeness data during the collection days, we create new functional variables that resembled in the best possible way the BADLs [18] and IADLs [19]. For the same reason, we need to unify all types of physical restraints data (i.e., double beds, corsage, wrist bands, etc.) in one variable, so the results might be overestimated. Lastly, we did not collect data regarding the main reasons of rehabilitation admission, thus preventing us to investigate the association of a specific with delirium.

Conclusion

In this multicenter study, we analyzed prevalence of delirium and its motor subtypes in a wide cohort of older persons admitted to IRFs, as well as factors associated with delirium. Our research also showed how relevant is the diagnosis of pre-existing dementia along with a thorough evaluation of the functional status and specific drug classes.

Further prospective investigations should be performed to expand scientific data about the prevalence and features of delirium in rehabilitation settings, to clarify the best approach for the prevention and management of delirium in a relatively understudied clinical setting.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40520-022-02099-8.

Acknowledgements The authors gratefully acknowledge the contributions of the Italian Study Group on Delirium (ISGoD) members who performed data collection and author's family members. The full list of ISGoD can be found in Supplementary Material.

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Author contributions All authors contributed to the conception and design of the study. CS, EM, MI, AC, AMa, AMo, GB: contributed to the acquisition of the data. AZ, ET and ER: were responsible for the statistical analysis and interpretation of the data. CS, AZ, AMo and GB: contributed to the draft of this paper. All authors have read, revised and approved the final manuscript.

Funding The authors did not receive support from any organization for the submitted work.

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

Declarations

Conflict of interest The authors have no competing interests to declare that are relevant to the content of this article.

Ethics approval The study protocol for Delirium day events were approved from the Ethical Committees of the IRCCS Fondazione Santa Lucia, Rome (year 2015) and of the University of Milano-Bicocca, Monza, Italy (years 2016–2017).

Statement of human and animal rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Consent to publish All participants gave their written informed consent prior to participation.

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