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Delirium at the intensive care unit and long-term survival: a retrospective study

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Abstract

Background Delirium is a common complication in patients at the intensive care unit (ICU) and is associated with prolonged ICU-stay and hospitalization and with increased morbidity. The impact of ICU-delirium on long-term survival is not clearly understood.

Methods This retrospective single center observational study was conducted at the Institute of Intensive Care Medicine at the University Hospital Zurich, Switzerland. All adult ICU-survivors over a four-year period were screened for eligibility. ICU-delirium was defined based on the Intensive Care Delirium Screening Checklist (ICDSC), together with the coded diagnosis F05 in the International Classification of Diseases (ICD-2019). ICU-survivors who developed delirium during their ICU stay (group D) were compared with ICU-survivors who did not (group ND). Survival was evaluated according to data from hospital electronic health records up to four years from ICU-discharge. The survival analysis was reported using Kaplan-Meier curves and absolute risk differences (ARD). A multivariable logistic regression model was fitted with long-term survival at four years after ICU-discharge as outcome of interest, including several clinical conditions and interventions associated with long-term survival for ICU patients. For subgroup analysis, ICU-survivors were grouped based on age at the time of admission (45–54, 55–64, ≥ 65 years), and on relevant clinical conditions.

Results A total of 9'604 patients fulfilled the inclusion criteria, of them 22.6% ($n = 2'171$) developed ICU-delirium. Overall, patients in the group D had a significantly lower probability of survival than patients in the group ND ($p < 0.0001$, ARD = 11.8%). In the multivariable analysis, ICU-delirium was confirmed as independently associated with long-term survival. After grouping for age categories, patients between 55 and 64 years of age in the group D were less likely to survive than patients in the group ND at every time point analyzed, up to four years after ICU discharge ($p < 0.001$, ARD = 7.3%). This difference was even more significant in the comparison between patients over 65 years ($p < 0.0001$, ARD 11.1%). No significant difference was observed in the other age groups.

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Conclusions In the study population, ICU-delirium was independently associated with a reduced long-term survival. Patients who developed ICU-delirium had a reduced survival up to four years after ICU discharge and this association was particularly evident in patients above 55 years of age.

Keywords Encephalopathy, Delirium, ICU, Long-term survival

Background

Delirium represents a common complication in patients treated at the intensive care unit (ICU), affecting approximately one third of the critically ill adults, with a prevalence that can reach the 80% among the mechanically ventilated patients [1, 2]. It is associated with prolonged ICU-, hospital-length of stay (LOS) [3, 4] and duration of mechanical ventilation [5], increased disability [6, 7], reduced long-term cognitive performance [8], as well as increased health care costs [9].

Available data on ICU-delirium and its association to short-term survival are discordant [3, 5, 10–13]. Considering the association between ICU-delirium and long-term survival, data are even more scare and not conclusive. A few studies reported an increased mortality in patients who developed delirium at 6-months [14], 1-year [15], and – in a population of only post-operative patients –even at 5-years [16], compared to patients who did not. On the contrary, in two prospective cohort studies no difference in 1-year mortality has been observed among patients who developed delirium and patients who did not [17, 18].

These discrepancies in the available data could be explained with methodological issues, such as the small sample size of the analyzed populations, the heterogeneity in the definition of delirium, different timing in the assessment of the possible association between delirium and mortality, as well as possible inclusion bias.

Our retrospective observational study focuses on the association between ICU-delirium and long-term survival. To do that, we applied a standardized definition of delirium based both on regular scoring and clinical judgment to a large population of ICU-patients and investigated survival at different time point: 1-year, 2-year, 3-year and up to 4-year following ICU-discharge.

Methods

This retrospective single center observational study was conducted at the Institute of Intensive Care Medicine at the University Hospital Zurich, Switzerland. All patients admitted to the ICU between January, 1st 2019 and December, 31st 2023 were screened for eligibility. Inclusion criteria were: (1) age ≥ 18 years old, (2) clinical diagnosis based on clinical judgment and coded according to the International Classification of Diseases (ICD-10, version 2019). Exclusion criteria were (1) patients' documented refusal to have their data analyzed for research projects; (2) no documented Intensive Care Delirium Screening Checklist (ICDSC) [19]; (3) ambiguous delirium status; (4) death at the ICU.

Data were obtained from the hospital electronic health records (KISIM-TM, Cistec, Zurich, Switzerland) and from the ICU Patient Data Management System (PDMS, MetaVision, iMDsoft, Israel). Collected data were: Demographics, including age and sex; SAPS II scores [20]; ICU- and hospital-length of stay (ICU-LOS, H-LOS); survival at different time points (at one, two, three and four years) after ICU-discharge. Moreover, to analyze the influence of other possible risk factors affecting long term survival in ICU patients, the following conditions or interventions, selected in the light of the available literature, were analyzed: diabetes [21], atrial fibrillation/flutter [22], acute respiratory failure and chronic obstructive pulmonary disease (COPD) [23], dementia [24], malignancies [25], hours of mechanical ventilation [26], need for renal replacement therapy [27] or need for hemodynamic mechanical support [28]. The main diagnosis for ICU admission were presented after grouping according to ICD-10 codes.

To define delirium and stratify the population accordingly, two criteria were considered: ICDSC score and clinical diagnosis. The ICDSC assessment is routinely performed three times a day by trained ICU-nurse staff and is considered positive if ≥ 4. If confirmed from the clinical judgment of the treating physician, a diagnosis of delirium is reported in the electronic medical records, coded according to ICD-10 as diagnosis F05 (delirium, not induced by alcohol and other psychoactive substances). ICU-Delirium patients (group D) were defined based on the above two complementary criteria: (1) at least one positive ICDSC assessment, and (2) the coded diagnosis F05. Likewise, non-delirious ICU patients (group ND) were defined as: (1) no positive ICDSC assessment, and (2) no coded F05 diagnosis. The ICU-delirium status of patients that fulfilled only one criterion was considered ambiguous, leading to exclusion of these patients.

The survival analysis was performed based on data from the electronic medical records. In the Canton Zurich, death certificates from the Civil Registry Department of the Municipal Office are automatically transferred into the patient's electronic record regardless of whether the death occurred in the hospital or not. The population of ICU survivors was arbitrary grouped in four age categories, also taking into account the age distribution in the population: 45–54 years, 55–64 years,

and ≥ 65 years. The cut-off for older adult patients was set at 65 years, being the 'retirement age' according to the Swiss federal social insurance system.

Statistical analysis

All statistical analyses were performed using the Scientific Python Development Environment Spyder IDE (Python 3.9.7 64-bit), and a p-value ≤ 0.05 was considered statistically significant. Descriptive statistics are reported as counts/percentages, mean ± standard deviation, or as median including the interquartile range, as appropriate. All continuous data were tested for normality using Shapiro–Wilk's test. Data not normally distributed were compared using the Mann–Whitney test. Numerical variables with normal distribution were compared using independent sample t test. Ordinal variables or numerical variables with not normal distribution were compared using Mann–Whitney-Wilcoxon test. Categorical variables were compared with chi-squared test. A multivariable logistic regression analysis was performed with covariates selected based on clinical relevance and prior evidence. The logistic regression model was fitted using the maximum likelihood estimation method, with the exposure variable and all covariates included in the model simultaneously. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. For the significant covariates, survival analysis was conducted using Kaplan-Meier curves, with significance between groups being assessed with the log-rank test. The Absolute Risk Difference (ARD) was calculated at specific time points by subtracting the survival probability of the delirium group from that of the non-delirium group.

Reporting of the study results adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [29].

Results

Overall, 16'557 patients were screened for eligibility. Of them 6'953 were excluded. Reasons for exclusion are listed in Fig. 1. In particular, 2'151 patients (11.9%) were excluded due to the missing coded diagnosis F05, and 465 patients (2.6%) due to the absence of a positive ICDSC score (Fig. 1).

The study population included 9'604 patients (females $n = 3'250$ (33.8%), median age: 63 years [IQR: 51, 72], median ICU-LOS: 1.8 days [IQR: 0.9–5.0]) (Table 1).

Most of these patients were admitted to the ICU due to a cardiovascular diagnosis (39.2%, $n = 3'763$), followed by onco-hematological diagnosis (17.0, $n = 1'629$), trauma (10.9%, $n = 1'048$), neurological disorders (6.5%, $n = 621$), and respiratory conditions (5.9%, $n = 565$) (Fig. 2).

Overall, 2'171 ICU-survivors (22.6%) developed delirium during their ICU stay (D = delirium group), while 7'433 (77.4%) did not (ND = non delirium group). In the

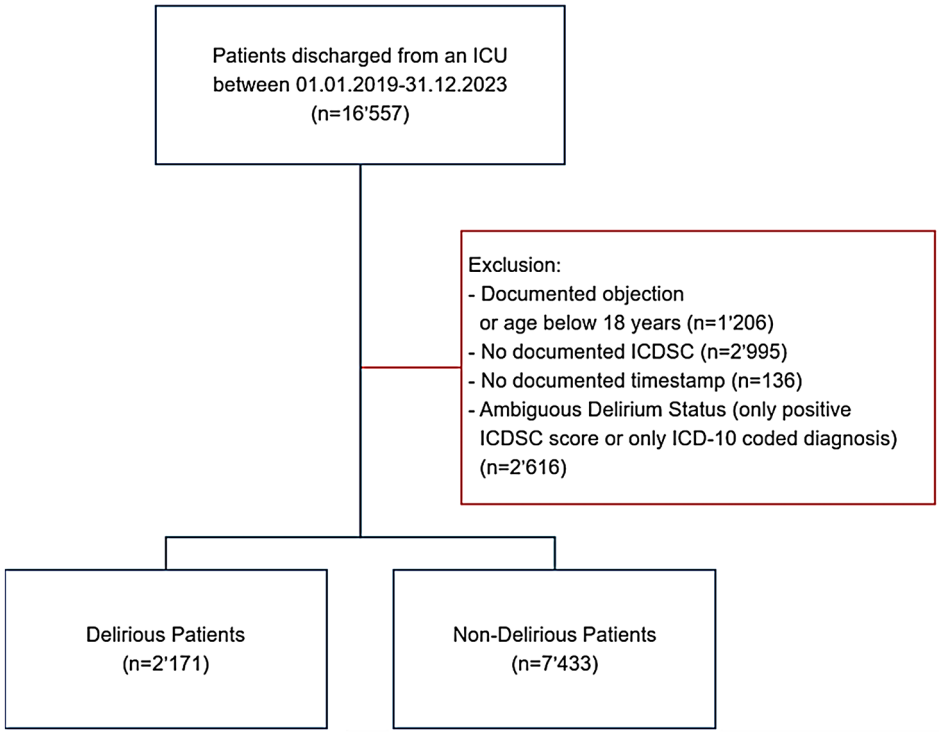

Fig. 1 Flow chart. Inclusion and exclusion criteria. study population flow chart. ICU: intensive care unit, ICDSC: Intensive Care Delirium Screening Checklis,; SAPS II: Simplified Acute Physiology Score II, ICD: International Classification of Diseases

Table 1 Baseline characteristics of the study population. (A) Demographics, pre-existing conditions and interventions (B) Major diagnostic categories. D: delirium group, ND: non-delirium group, ICU: Intensive Care Unit, SAPS II: Simplified Acute Physiology Score II, IQR: interquartile range, COPD: chronic obstructive pulmonary disease

A. Demographics, pre-existing conditions and interventions				
	General population (D & ND)	**Statistical analysis between D & ND groups**		
		D	**ND**	**• *p*-value**
N of total Patients	9'604	2'171	7'433	-
Females, n (%)	3'250 (33.8)	626 (28.8)	2'624 (35.3)	< 0.0001
Age, median (IQR)	63.0 (51.0, 72.0)	68.0 (58.0, 77.0)	61.0 (49.0, 71.0)	< 0.0001
SAPS II, median (IQR)	35.0 (25.0, 47.0)	• 47.0 (37.0, 59.0)	32.0 (22.0, 43.0)	< 0.0001
ICU length of stay [days], median (IQR)	1.8 (0.9, 5.0)	8.7 (4.0, 17.0)	1.0 (0.8, 2.6)	< 0.0001
Hospital length of stay [days], median (IQR)	11.3 (7.6, 18.6)	20.4 (12.8, 32.1)	10.0 (6.9, 15.0)	< 0.0001
Hospital deaths, n (%)	222 (2.0)	96 (4.1)	126 (1.5)	< 0.0001
Mechanically ventilated, n (%)	8'322 (86.6)	1'986 (91.5)	6'336 (85.2)	0.006
Mechanical Ventilation [days], median (IQR)	0.4 (0.2, 1.02)	2.1 (0.5, 6.4)	0.3 (0.2, 0.5)	< 0.0001
Malignancies, n (%)	1'476 (15.4)	214 (9.9)	1'262 (17.0)	< 0.0001
Acute Respiratory Failure, n (%)	795 (8.3)	286 (13.2)	509 (6.8)	< 0.0001
COPD, n (%)	600 (6.2)	193 (8.9)	407 (5.5)	< 0.0001
Atrial Fibrillation / Flutter, n (%)	1'790 (18.6)	659 (30.4)	1'131 (15.2)	< 0.0001
Diabetes, n (%)	1'488 (15.5)	443 (20.4)	1'045 (14.0)	< 0.0001
Dementia, n (%)	171 (1.8)	66 (3.0)	46 (0.6)	< 0.0001
Hemodynamic mechanical support, n (%)	522 (5.4)	361 (16.6)	161 (2.2)	< 0.0001
Renal replacement therapy, n (%)	293 (3.0)	204 (9.4)	89 (1.2)	< 0.0001
B. Diagnostic Categories of ICU Admission				
Cardiovascular system, n (%)	3'763 (39.2)	869 (40.0)	2'894 (38.9)	0.474
Oncology & Hematology, n (%)	1'629 (17.0)	159 (7.3)	1'470 (19.8)	< 0.0001
Others, n (%)	1'271 (13.2)	277 (12.8)	989 (13.3)	0.381
Trauma, n (%)	1'048 (10.9)	372 (17.1)	677 (9.1)	< 0.0001
Neurological system, n (%)	621 (6.5)	113 (5.2)	508 (6.8)	0.009
Respiratory system, n (%)	565 (5.9)	148 (6.8)	417 (5.6)	0.041
Digestive system, n (%)	383 (4.0)	108 (5.9)	275 (3.7)	0.009
Infectious & Parasitic Diseases, n (%)	323 (3.4)	125 (5.8)	198 (2.7)	< 0.0001

D group, females were fewer (28.8% vs. 35.3%, $p < 0.001$) and patients were older (median age 68 [IQR: 58, 77] vs. 61 [IQR: 49, 71], $p < 0.001$). The median SAPS II was 35 points [IQR: 25, 47]. Patients in the D group had a higher SAPS II score than those in the ND group (median SAPS II score 47 [IQR: 37, 59] vs. 32 [IQR: 22, 43], $p < 0.001$).

Considering outcomes, patients in the D group had a longer ICU-, as well as hospital-LOS (median stay: 8.7 days [IQR: 4.0, 17.0] vs. 1.0 days [IQR: 0.8, 2.6], $p < 0.001$ and 20.4 days [IQR: 12.8, 32.1] vs. 10.0 days [IQR: 6.9, 15.0], $p < 0.001$ respectively) then patients in the ND group (Table 1). After discharge from the ICU, 2% of the patients ($n = 222$) died during their hospital stay (D group: $n = 96$, 4.1%; ND group: $n = 126$, 1.5%, $p < 0.0001$).

The analysis of comorbidities and interventions showed that more patients in the D group were mechanically ventilated (91.5%, $n = 1'968$ vs. 85.2%, $n = 6336$, $p = 0.006$), and for longer time (2.1 days, [IQR: 0.5–6.4] vs. 0.3 days [IQR: 0.2–0.5]). As pre-existing conditions, delirious patients had more acute respiratory failure (13.2% vs. 6.8%, $p < 0.001$), COPD (8.9% vs. 5.5%, $p < 0.001$), atrial fibrillation (30.4% vs. 15.2%, $p < 0.001$), diabetes (20.4% vs. 14.0%. $p < 0.001$), and dementia (3.0% vs. 0.6%, $p < 0.001$). On the contrary, patients in the D group had fewer pre-existing malignancies then patients in the ND group (9.9% vs. 17.9%, $p < 0.001$). Regarding interventions, delirious patients received more hemodynamic mechanical support (16.6% vs. 2.2% $p < 0.001$) and renal replacement therapy (9.4% vs. 1.2%, $p < 0.001$) (Table 1-B).

In the multivariable logistic regression model, ICU-delirium was independently associated with reduced survival at 4 years after ICU discharge (OR: 1.41, 95%CI 1.26–1.86, $p < 0.001$) (Table 2; Fig. 3).

Throughout the observational time window of four years, patients in the D group had a significantly lower probability of survival than patients in the ND group

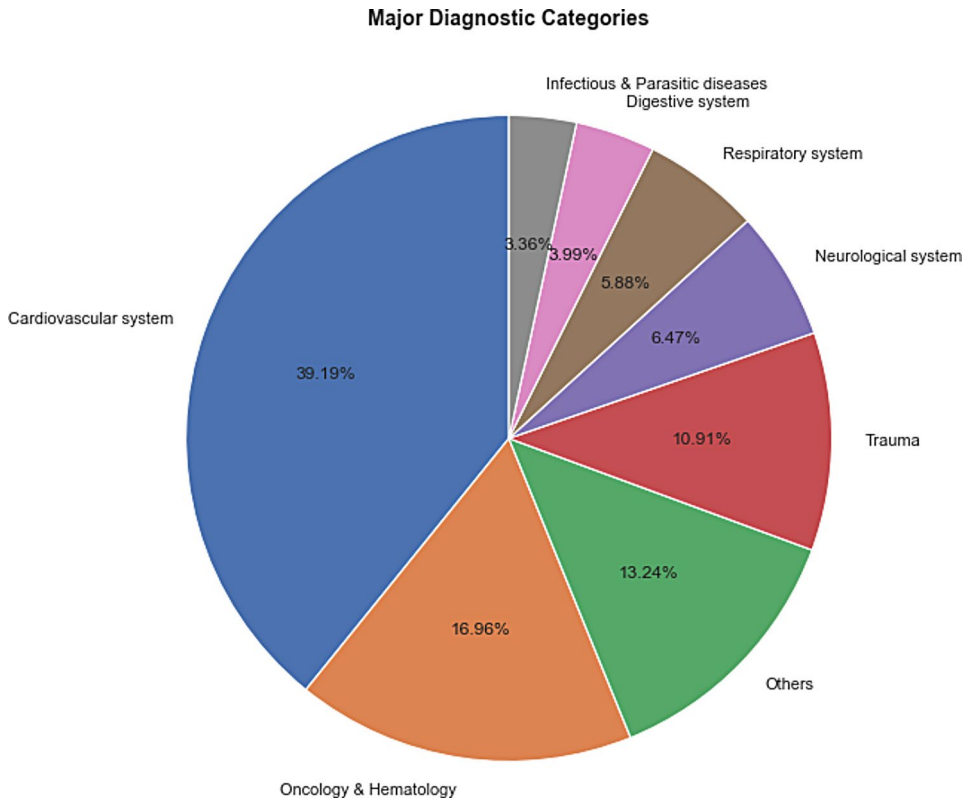

Fig. 2 Diagnostic Categories of ICU Admission. Pie chart illustrating the distribution of the study population according to the main diagnosis for ICU admission as coded with the ICD-10

Table 2 Multivariable logistic regression model. Long-term survival at 4 years was considered as outcome. Y/N: yes/no, M/F: male/female, ICU-LOS: intensive care unit - length of stay, COPD: chronic obstructive pulmonary disease, OR: odds ratio, CI: confidence interval

Variable	Coefficient	*p*-value	OR (95% CI)
Acute respiratory failure (Y/N)	-0.44	< 0.0001	0.65 (0.53, 0.79)
Hemodynamic mechanical support (Y/N)	-0.13	0.547	0.88 (0.58, 1.34)
Diabetes (Y/N)	-0.05	0.496	0.95 (0.82, 1.10)
Sex (M/F)	-0.04	0.510	0.96 (0.86, 1.08)
Atrial fibrillation/Flutter (Y/N)	-0.01	0.851	0.99 (0.86, 1.13)
ICU-LOS (days)	0.01	0.014	1.01 (1.00, 1.01)
Mechanical ventilation (days)	0.02	0.012	1.02 (1.00, 1.03)
Delirium (Y/N)	0.34	< 0.0001	1.41 (1.23, 1.62)
Age (/10 years)	0.41	< 0.0001	1.50 (1.44, 1.56)
COPD (Y/N)	0.43	< 0.0001	1.53 (1.26, 1.86)
Renal replacement therapy (Y/N)	0.71	< 0.0001	2.03 (1.63, 2.53)
Dementia (Y/N)	0.77	0.0002	2.16 (1.45, 3.22)
Malignancy (Y/N)	1.51	< 0.0001	4.52 (3.99, 5.13)

(Fig. 4). After grouping for age categories, among patients between 45 and 54 years, no differences in the survival curves were observed in patients in the D and ND groups ($p = 0.607$) (Fig. 4-B). Among patients between 55 and 64 years, patients in the D group were less likely to survive than patients in the ND group ($p = 0.0003$, ARD = 7.3%) (Fig. 4-C). This difference was even more evident among patients older than 65 years ($p < 0.0001$, ARD = 11.1%) (Fig. 4-D) (Table 2). Moreover, for each condition or intervention with significant contribution in the multivariable model, survival was significantly lower in the D group with the exception of COPD and dementia (Fig. 4E-J).

Discussion

Our study investigates a possible association between ICU-delirium and long-term survival in a large population of ICU survivors. As the main finding, we report that ICU survivors over 55 years of age who suffered from delirium during their ICU stay had a lower survival over time up to four years from ICU discharge compared to patients who did not.

To date, only few studies analyzed long-term outcomes related to ICU-delirium, and methodological issues limit these previous works [15–18]. Similar to our findings, Moskowitz et al. observed an increased 5-years

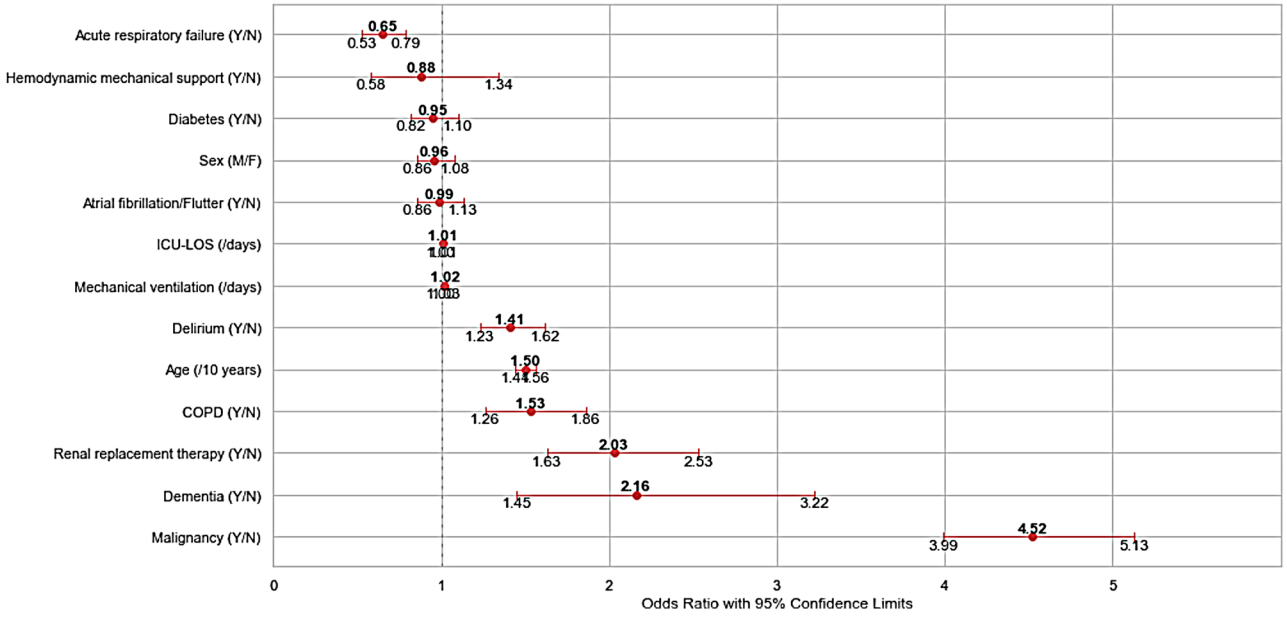

Fig. 3 Forrest plot with OR and 95% CI for different factors associated with long term survival at 4 years after ICU-discharge. Y/N: yes/no, M/F: male/female, ICU-LOS: intensive care unit - length of stay, COPD: chronic obstructive pulmonary disease, OR: odds ratio, CI: confidence interval

mortality in patients with ICU-delirium. However, this study only included patients over 50 years of age admitted to the ICU after elective surgery [16], which limits the generalization of the findings. Pisani et al. reported an association between ICU-delirium duration and 1-year mortality. In this study, the generalization of the finding is limited by including only older adult patients (over 65 years of age) [15]. On the contrary, Wolters et al. could not confirm an association between ICU-delirium and 1-year mortality [17]. The population investigated, however, was small and patients with neurological conditions were excluded due to possible confounding factors. Additionally, in this previous study, delirium was defined only based on a positive score – CAM-ICU – and/or administration of haloperidol [17]. The choice of this definition lacks, in our opinion, clinical judgment. Indeed, there are clinical conditions that could result in a positive CAM-ICU or ICDSC score for delirium without the patient actually having it. More recently, Fiest et al. performed a similar analysis on a larger population and, similarly to the work of Wolters et al., defined delirium based only on a score – in this case the ICDSC ≥ 4. Also in this study, no association was found between ICU-delirium and long-term survival [18].

In our study, we provide evidence for an association between ICU-delirium and long-term survival up to four years.

In our cohort, ICU-survivors who developed delirium during their ICU stay were significantly older than patients who did not. This finding is confirmatory, since increasing age is a known risk factor for delirium [30]. To exclude the association between ICU-delirium and long-term survival being due only to age differences, we conducted the survival analyses grouping the population by age. We found that ICU survivors above 55 years of age are those in whom the effect of ICU-delirium has the greatest impact on survival, and therefore worthy of further investigation – for example – for targeted prevention.

Moreover, in our cohort, patients with ICU-delirium had a higher median SAPS II score than patients who did not. One might therefore assume that patients with delirium have a lower survival also because they have a more severe clinical condition at ICU-admission.

However, two important aspects should be considered: firstly, the SAPS II is a score used to predict mortality in the ICU and not validated to predict long-term survival [20]. In our case, given the selected population of ICU survivors, the score would lose its applicability. Secondly, the SAPS II is inaccurate in patients with delirium. In fact, one of the items of the SAPS II score is the assessment of the Glasgow Coma Scale (GCS). In ICU patients with delirium, the GCS is very often reduced. In this case, the predictive value of the SAPS II is poor [31]. Therefore, to exclude possible confounding factors affecting ICU long-term survival, several pre-existing comorbidities or interventions affecting ICU long term survival were analyzed in the light of the available literature on the topic [21–28] and introduced in the multivariable logistic regression model with survival at 4 years after ICU-discharge as outcome of interest.

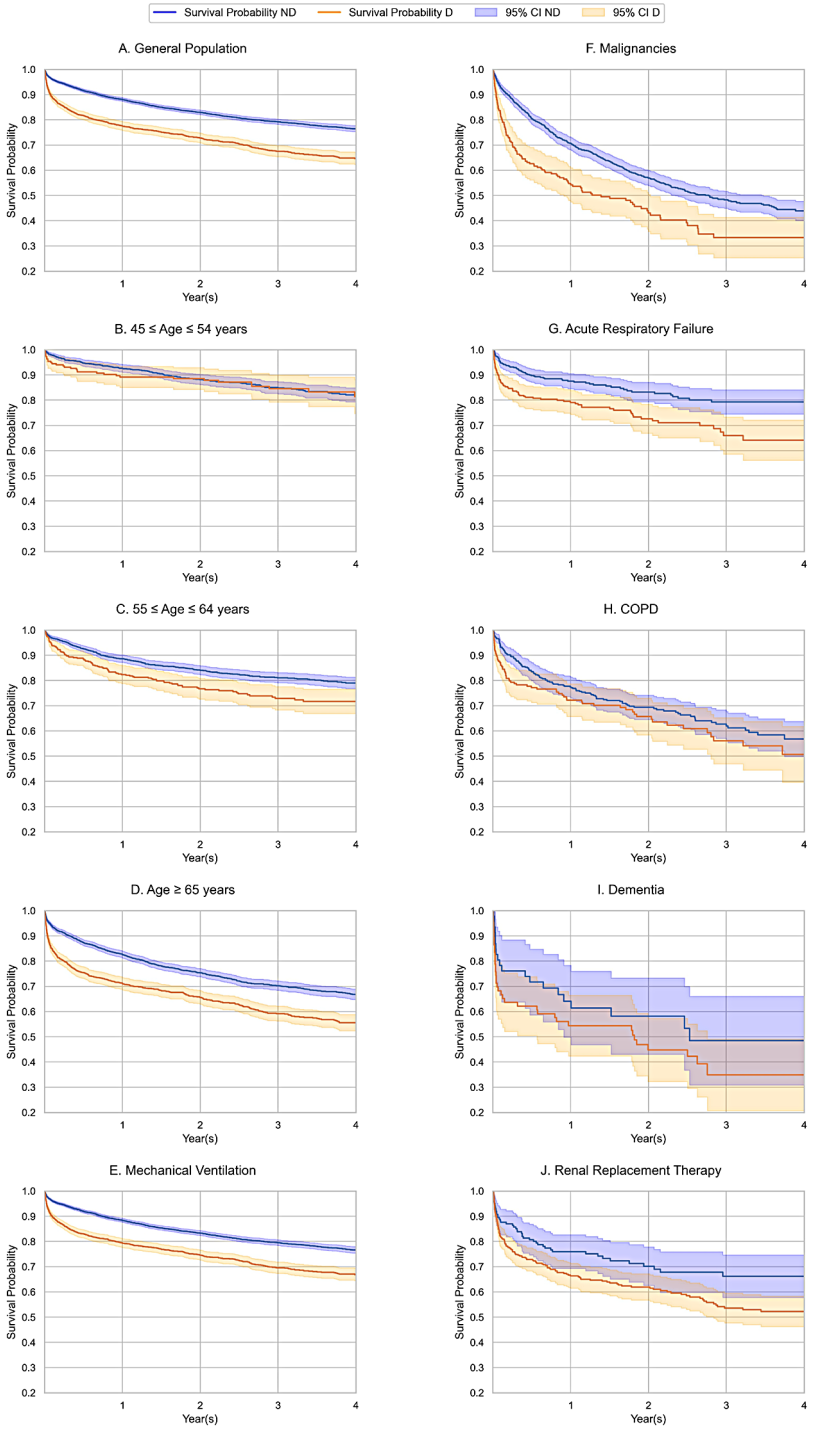

Fig. 4 Survival analysis of patients in the ND and D group illustrated by Kaplan-Meier plots. **A**. Survival analysis for the study population. **B**.Ppatients between 45 and 54 years. **C**. Patients between 55 and 64 years. **D**. Patients aged ≥ 65 years. **E**. Mechanically ventilated patients. **F** Patients with malignancies. **G** Patients with acute respiratory failure. **H**. Patients with COPD. **I.** Patients with pre-existing dementia. **J**. Patients undergoing renal replacement therapy. ND: non-delirium group, D: delirium group, CI: confidence interval, COPD: chronic obstructive pulmonary disease

The multivariable logistic regression model confirmed that ICU-delirium is independently associated with reduced long-term survival. This effect on the survival is more evident in the first year after ICU discharge but it persists at all the analyzed time points.

Our paper has several strengths: firstly, data on long-term survival for patients with ICU-delirium are scarce

Table 3 Number of patients at risk and absolute risk difference (ARD). Number of ICU survivors at risk and absolute risk difference (ARD) **A**. for the general population, **B-D**. After grouping by age, **E-J**.By different clinical conditions or interventions. Survival is assessed up to 4 years after ICU-discharge. N: number, ARD: absolute risk difference, ND: non-delirium group, D: delirium group, COPD: chronic obstructive pulmonary disease

		Years from ICU discharge									p-value Log-rank test
		0	1		2		3		4		
		N patients	N patients	ARD	N patients	ARD	N patients	ARD	N patients	ARD	
A. General population	D	2'171	1'453	0.106	1'026	0.102	671	0.117	332	0.118	< 0.0001
	ND	7'433	5'616		3'913		2'562		1'396		
B. Patients 45 ≤ age ≤ 54 years	D	216	167	0.034	134	0.004	83	0.003	44	0.007	0.6071
	ND	1'129	915		659		464		255		
C. Patients 55 ≤ age ≤ 64 years	D	448	316	0.063	219	0.073	143	0.082	66	0.073	0.0003
	ND	1'829	1'385		971		622		341		
D. Patients ≥ 65 years	D	1'296	807	0.116	561	0.098	375	0.111	183	0.111	< 0.0001
	ND	3'035	2'133		1416		901		490		
E. Mechanical ventilation	D	1'986	1'364	0.090	961	0.088	633	0.099	315	0.098	< 0.0001
	ND	6'336	4'766		3'280		2'142		1'185		
F. Malignancies	D	214	97	0.165	49	0.138	22	0.150	5	0.106	< 0.0001
	ND	1'262	759		415		216		64		
G. Acute respiratory failure	D	286	172	0.084	97	0.106	46	0.133	4	0.152	0.0002
	ND	509	259		150		87		11		
H. COPD	D	193	111	0.052	63	0.037	31	0.059	8	0.061	0.178
	ND	407	265		154		84		19		
I. Dementia	D	66	33	0.097	21	0.134	8	0.136	2	0.136	0.201
	ND	46	24		15		8		3		
J. Renal replacement therapy	D	361	201	0.096	139	0.082	89	0.126	50	0.140	0.018
	ND	161	101		62		41		25		

and we add evidence on it. Secondly, we decided to perform our survival analysis only on ICU survivors. This choice was justified by the fact that in patients who died at the ICU, a negative delirium score could be due to the extreme severity of the initial clinical condition rather than to an actual absence of delirium. Thirdly, we adopted a standardized definition of delirium based not only on the ICDSC delirium score, but also on the confirmation of the diagnosis through clinical judgement, as ultimately expressed by the ICD-10 coding. The ICDSC score has a pooled sensitivity of 0.83 and a specificity of 0.87 [32, 33]. The two complementary criteria allowed us to improve our specificity excluding those patients who, even presenting a positive ICDSC, were not considered by the clinician to have delirium. Fourthly, we performed the survival analysis grouping the patients by age and according to possible confounding factors that have already been demonstrated to have an association with long term survival after ICU. Lastly, our study is, to the best of our knowledge, the first one to analyze in a large patient population the association of ICU delirium and survival with a long-term follow-up of up to four years.

Some limitations need to be mentioned. Our analysis is in fact limited by the monocentric and retrospective nature of the study, which possibly reduce the generalizability of the results. Moreover, the grouping by age and the selection of comorbidities and interventions in the analysis was based on the available literature and this does not completely exclude a selection bias. We also recognize that in the definition of the delirious patients, the clinical judgment is subjective and, ultimately, a further selection bias cannot be excluded. Furthermore, the difference in the ICU- and hospital-length of stay between groups may rise some concerns leading to possible inclusion bias. However, ICU-LOS was considered in the multivariable logistic regression model and ICU-delirium still remained independently associated with long-term mortality.

Conclusion

In the study population, ICU-delirium was independently associated with reduced long-term survival. Patients who developed ICU-delirium had a reduced survival up to four years after ICU discharge and this association was particularly evident in patients above 55 years of age.

These discrepancies in the available data could be explained with methodological issues, such as the small sample size of the analyzed populations, the heterogeneity in the definition of delirium, different timing in the assessment of the possible association between delirium and mortality, as well as possible inclusion bias.

Our retrospective observational study focuses on the association between ICU-delirium and long-term survival. To do that, we applied a standardized definition of delirium based both on regular scoring and clinical judgment to a large population of ICU-patients and investigated survival at different time point: 1-year, 2-year, 3-year and up to 4-year following ICU-discharge.

Abbreviations

ICU	Intensive Care Unit
LOS	Length of stay
ICDSC	Intensive Care Delirium Screening Checklist
SAPS II	Simplified Acute Physiology Score II
PDMS	Patient Data Management System
ICU-LOS	Intensive Care Unit – Length of stay
H-LOS	Hospital – Length of stay
ICD	International Classification of Diseases
IQR	Interquartile range
ARD	Absolute Risk Difference
D	Delirium group
ND	Non-delirium group
CAM-ICU	Confusion Assessment Method – Intensive Care Unit
GCS	Glasgow Coma Scale
COPD	Chronic Obstructive Pulmonary Disease

Supplementary Information

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Supplementary Material 1

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Author contributions
ID, MAK, JB and GB designed the study. JB and GB supervised the study. ID and GB wrote the initial draft. MAK and JB performed the analysis and created tables and figures. EJ and RS gave critical input to the manuscript. All authors read and approved the final version of the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study was approved by the cantonal ethics committee of Zurich (BASEC: 2020–02695). The study complies with the Declaration of Helsinki, the Guidelines on Good Clinical Practice (GCP-Directive) issued by the European Medicines Agency as well as with Swiss law and regulatory authority requirements.

Consent for publication
Informed consent was obtained from the patients or from their relatives whenever possible. The cantonal ethics committee of Zurich granted permission to use the data of all patients who did not object to the use of their data for research purposes.

Competing interests
The authors declare no competing interests.

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