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Delirium at the end of life

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Abstract

Background. The general in-hospital mortality and interrelationship with delirium are vastly understudied. Therefore, this study aimed to assess the rates of in-hospital mortality and terminal delirium.

Method. In this prospective cohort study of 28,860 patients from 37 services including 718 in-hospital deaths, mortality rates and prevalence of terminal delirium were determined with simple logistic regressions and their respective odds ratios (ORs).

Results. Although overall in-hospital mortality was low (2.5%), substantial variance between services became apparent: Across intensive care services the rate was 10.8% with a 5.8-fold increased risk, across medical services rates were 4.4% and 2.4-fold, whereas at the opposite end, across surgical services rates were 0.7% and 87% reduction, respectively. The highest in-hospital mortality rate occurred on the palliative care services (27.3%, OR 19.45). The general prevalence of terminal delirium was 90.7% and ranged from 83.2% to 100%. Only across intensive care services (98.1%, OR 7.48), specifically medical intensive care (98.1%, OR 7.48) and regular medical services (95.8%, OR 4.12) rates of terminal delirium were increased. In contrast, across medical services (86.4%, OR 0.32) and in particular oncology (73.9%, OR 0.25), pulmonology (72%, OR 0.31) and cardiology (63.2%, OR 0.4) rates were decreased. For the remaining services, rates of terminal delirium were the same.

Significance of results. Although in-hospital mortality was low, the interrelationship with delirium was vast: most patients were delirious at the end of life. The implications of terminal delirium merit further studies.

Introduction

Delirium is the most common neuropsychiatric disorder in the medical setting and characterized by abrupt and fluctuating disturbances in alertness or attention and cognition caused by underlying etiologies (American Psychiatric Association, 2013).

The general prevalence rate of delirium across hospital settings has been estimated to be 20%, reaching 24% depending on the setting (Ryan et al., 2013; Meagher et al., 2014; Bellelli et al., 2016; McCoy et al., 2017). However, as has been shown in palliative care patients, this rate, termed terminal delirium, can exceed 90% in the dying (Lawlor et al., 2000; Weckmann et al., 2014; Maldonado, 2017; Watt et al., 2019). Delirium is common at the end of life, in particular during the last 24–48 h (Harris, 2007). Thus, it is safe to assume a strong interrelationship of delirium and death generalizing to all dying patients.

Further, delirium can cause adverse experiences, i.e., the delirium experience (Grover and Shah, 2011; Partridge et al., 2013; Grover et al., 2015; Schmitt et al., 2019). This experience is associated with substantial suffering for patients and can even cause posttraumatic symptomatology. Whether this experience also applies to terminal delirium is unknown.

To date, the rate of terminal delirium has not yet been determined beyond a palliative care setting. Therefore, this prospective cohort study aimed to explore the interrelationship of delirium and death across all services, medical, surgical, intermediate, and intensive care.

Methods

Patients and procedures

All data in this prospective cohort derived from the DelirPath (Schubert et al., 2018), a quality improvement initiative aiming to improve the detection and management of delirium in all hospitalized patients, running from January 1 to December 31, 2014 at the University Hospital Zurich, a tertiary care center.

In total, 39,442 patients were admitted and registered in the DelirPath. After applying the exclusion criteria: age <18, length of stay (LOS) <1 day, the combination of age and LOS and

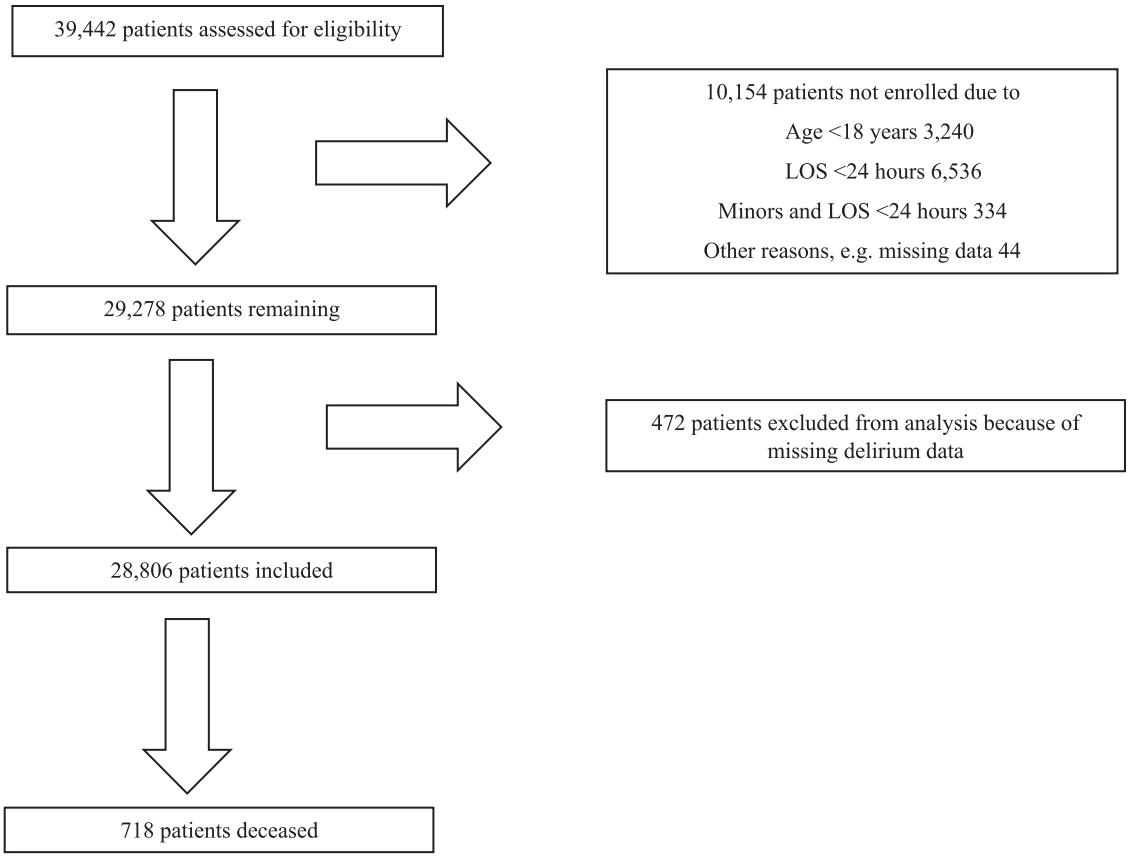

Fig. 1. Flow diagram of patient selection.

missing data, including the electronic patient assessment – acute care (ePA-AC), 28,860 patients from 37 services were included in the analysis (Figure 1).

The detection of delirium was based on the Delirium Observation Screening Scale (DOS; Schuurmans et al., 2003), Intensive Care Delirium Screening Checklist (ICDSC; Bergeron et al., 2001), and the Diagnostic and Statistical Manual (DSM)-5 relevant parameters of the ePA-AC (Hunstein et al., 2012). On regular floors, the DOS was administered thrice daily during the first three days of admission in patients <65 years or based on suspicion of incident delirium for patients of all ages. Once delirium occurred, the DOS was continued thrice daily until remission. On the ICUs, the ICDSC was routinely performed thrice daily and the ePA-AC was routinely performed daily in all hospitalized patients.

These instruments were performed by nursing staff trained via eLearning, literature research, 4-h courses, case reports, and final exams.

Of the respective managing departments, DOS or ICDCS and ePA-AC scores were automatically retrieved from the electronic medical chart (Klinikinformationssystem, KISIM, CisTec AG, Zurich).

All reporting followed the STROBE statement (Vandenbroucke et al., 2014). This study was approved by the ethics committee of the Canton of Zurich (KEK-ZH-Nr. 2012-0263). A waiver of informed consent was obtained from the committee.

The purpose of this study was to assess in-hospital mortality and delirium at the end of life across services.

Determination of delirium

The primary evaluation of delirium was based on the DOS (Schuurmans et al., 2003), ICDSC (Bergeron et al., 2001), and DSM-5 construct based on the ePA-AC (Hunstein et al., 2012).

The DOS is a 13-item scale validated to indicate delirium according to DSM-IV criteria and rated as not existent (0), sometimes to always existent (1), and unable to assess (–). Items include disturbances of consciousness (1), attention (2–4), thought processes (5 and 6), orientation (7 and 8), memory (9), psychomotor behavior (10, 11, and 13), and affect (12). The cutoff score for delirium is ≥3 and values were aggregated throughout recordings.

The ICDSC is an eight-item screening instrument based on DSM-IV criteria, specifically designed for the intensive care setting, rating patient behaviors over the previous 8 h with two points: absent or present. Items assess consciousness (1 — comatose, soporose, awake, or hypervigilant), orientation (2), hallucinations or delusions (2), psychomotor activity (4), inappropriate speech or mood (5), attentiveness (6), sleep–wake cycle disturbances (7), and fluctuations in symptomatology (8). The cutoff score for delirium is ≥4 and values were aggregated throughout recordings.

The ePA-AC is a nursing instrument administered daily assessing mobility, personal care and dressing, feeding, elimination, cognition and alertness, communication and interaction, sleeping, breathing, pain, pressure ulcers, and wounds. The DSM-5 based items representing alertness or inattention and cognition were considered for measuring delirium and aggregated throughout recordings.

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Definition of terminal delirium

For the purpose of this study, terminal delirium was defined as the coincidence of delirium and subsequent death.

Statistical methods

Data analyses were performed with the Statistical Package for the Social Sciences (SPSS) version 25 and R statistical software version 3.5.0 for Windows.

Descriptive characteristics were summarized as percentages for categorical variables.

In a first step, the data were dichotomized by mortality and managing service. Then, simple logistic regressions with Pearson's χ^2 or Fisher's exact test where appropriate were calculated to determine the mortality rates with the respective odds ratios (ORs) and confidence intervals (CIs). Then, all services with absent mortality rate were omitted. In a second step, mortality was selected and patients dichotomized by the presence or absence of delirium and split into managing services and the same statistical procedures as described in step one was applied. *P*-values were adjusted for multiple testing using the false discovery rate (Benjamini and Hochberg, 1995).

For all inferential tests, two-tailed tests were chosen and the significance level alpha (α) was set at $P < 0.05$.

Results

Mortality rates across services

Overall, mortality rate was a modest 2.5% across the hospital, with, however, notable outliers, which were the ICUs (10.8%), followed by medical services (4.4%), IMCs (3.1%), and surgical services (0.7%). Hence, the mortality risk was increased on the ICUs (OR 5.97) and medical services (OR 2.4), although decreased on the surgical services (OR 0.13) (Table 1).

Generally, in the medical services, mortality rates were low; however, distinct outliers were noted: expectedly, mortality in palliative care reached 27.3% being the highest among services, followed by oncology with 8.1%. Most medical services ranged between 1% and 5%. At the low end were rheumatology with 0.3% and endocrinology where no patient had died. Similarly, the associations between mortality and services were greatest for palliative care (OR 19.45), oncology (OR 3.94), internal medicine (OR 3.54), hematology (OR 2.06), and gastroenterology (OR 2.05). Medical services with weak associations were rheumatology (OR 0.13), angiology (OR 0.28), and neurology (OR 0.4).

Mortality rates were lower in the surgical services regular floors than in medical ones. On cardiac surgery, mortality reached 2.9% displaying the strongest association with mortality (OR 1.8). On most surgical services, mortality rates ranged between 0.4% and 1.3%. In particular, weak associations between mortality and service were noted for otorhinolaryngology (OR 0.08), neurosurgery (OR 0.15), gynecology, plastic surgery, and urology (all OR 0.16), thoracic surgery (OR 0.45), dermatology (OR 0.52), and visceral surgery (OR 0.53).

Contrarily, on the intermediate and intensive cares services mortality rates were substantial, although not reaching the rate in palliative care. In the descending order, these rates reached 20.1% on the medical ICU, 17.3% in the visceral–thoracic–transplant ICU, 13% on the cardiovascular surgical ICU, 11.2% on the trauma SICU, and 10.1% on the neurosurgical ICU. Conversely, the lowest rate was observed on the stroke unit with 3.8%.

Table 1. Mortality rates across various medical, surgical, intermediate, and intensive care services

	Mortality rate in %	*P*, OR, CI
All medical	**4.4**	**<0.001, 2.4, 2.07–2.79**
Angiology	0.7	0.011, 0.28, 0.09–0.86
Cardiology	1.7	0.433
Endocrinology	–	–
Gastroenterology	4.3	<0.001, 2.05, 1.45–2.9
Geriatrics	3.6	–
Hematology	4.4	0.001, 2.06, 1.36–3.13
Infectiology	1.7	–
Internal Medicine	3.8	<0.001, 3.54, 2.87–4.37
Nephrology	4.2	0.109
Neurology	1.3	0.013, 0.4, 0.19–0.84
Oncology	8.1	<0.001, 3.94, 3.07–5.06
Palliative Care	27.3	<0.001, 19.45, 15.5–24.41
Pulmonology	3.8	0.003, 1.76, 1.21–2.56
Rheumatology	0.3	<0.001, 0.13, 0.32–0.52
All surgical	**0.7**	**<0.001, 0.13, 0.11–0.16**
Cardiac surgery	2.9	<0.001, 1.8, 1.37–2.36
Ophthalmology	1.3	0.020, 0.52, 0.3–0.91
Dermatology	–	–
Gynecology	0.4	<0.001, 0.16, 0.08–0.31
Neurosurgery	0.7	<0.001, 0.15, 0.05–0.46
Obstetrics	–	–
Orofacial surgery	–	–
Otolaryngology	0.2	<0.001, 0.08, 0.03–0.21
Plastic surgery	0.2	<0.001, 0.16, 0.06–0.43
Thoracic surgery	1.1	0.025, 0.45, 0.21–0.94
Trauma	1.8	1
Urology	0.4	<0.001, 0.16, 0.08–0.34
Visceral surgery	1	0.002, 0.53, 0.35–0.8
All IMC	**3.1**	**0.464**
Abdominal	–	–
Cardiothoracic	1.2	0.111
Stemcell transplant	3.5	0.118
Stroke	3.8	0.048, 1.53, 1.01–2.32
All IPS	**10.8**	**<0.001, 5.97, 5.05–7.05**
Burn	8.4	0.001, 3.59, 1.87–6.88
Cardiovascular	13	<0.001, 5.97, 3.86–9.23<0.001,
Medical	20.1	<0.001, 10.68, 8.14–14.01
Neurosurgery	10.1	4.49, 3.13–6.46
Trauma	11.2	<0.001, 5.07, 3.54–7.27
Visceral–thoracic	17.3	<0.001, 8.34, 5.5–12.77

OR, odds ratio; CI, confidence interval.

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Similarly, in the descending order, the association with mortality was strongest on the medical ICU (OR 10.68), the visceral–thoracic–transplant ICU (OR 8.34), the cardiovascular surgical ICU (OR 5.97), the trauma SICU (OR 5.07), neurosurgical ICU (OR 4.49), and weakest on the stroke unit (OR 1.53).

Mortality associated with delirium across managing services

Generally, prevalence rates of terminal delirium were substantial throughout services: pooled across settings 90.7%, in the ICUs 98.1%, in the IMCs 95.2%, in the surgical services 89.7%, and in the medical services 86.4%. Hence, the risk for terminal delirium was increased on the ICUs (OR 7.48) and decreased on the medical services (OR 0.32) (Table 2).

With such high rates of terminal delirium with a small range, only few findings reached significance. Among medical services reaching a rate of 100% were angiology, geriatrics, infectiology, nephrology, neurology, and rheumatology. However, in part, mortality rates were low on these services. Only on the medical services, the risk for terminal delirium was increased (OR 4.12), whereas on cardiology (OR 0.4), pneumonology (OR 0.31), and oncology (OR 0.25), the risk was decreased.

Of the surgical and intermediate care services, rates of 100% terminal delirium were reached on dermatology, neurosurgery, plastic and visceral surgery, as well as stem cell transplant and stroke units. Intergroup differences for terminal delirium did not exist.

For the ICUs, the visceral–thoracic–transplant and burn unit reached 100% terminal delirium and — beyond the generally increased risk for delirium — only the medical ICU with 98.6% terminal delirium and eightfold increased risk for terminal delirium stood out.

Table 2. Terminal delirium rates across various medical, surgical, intermediate, and intensive care services

	Delirium rate in %	*P*, OR, CI
All medical	**86.4**	**<0.001, 0.32, 0.18–0.57**
Angiology	100	–
Cardiology	63.2	0.031, 0.4, 0.18–0.86
Gastroenterology	88.9	1
Geriatrics	100	–
Hematology	90.5	1
Infectiology	100	–
Internal Medicine	95.8	0.007, 4.12, 1.27–13.37
Nephrology	100	–
Neurology	100	–
Oncology	73.9	<0.001, 0.25, 0.14–0.46
Palliative Care	91.3	0.605
Pulmonology	72	0.015, 0.31, 0.13–0.76
Rheumatology	100	–
All surgical	**89.7**	**0.726**
Dermatology	100	–
Cardiac surgery	83.3	0.634
Gynecology	77.8	0.200
Neurosurgery	100	–
Otolaryngology	66.7	0.323
Plastic surgery	100	–
Thoracic surgery	83.3	1
Trauma	90	1
Urology	83.3	0.131
Visceral surgery	100	–
All IMCs	**95.2**	**0.527**
Cardiothoracic	95.2	0.711
Stem cell transplant	100	–
Stroke	100	–
All ICUs	**98.1**	**<0.001, 7.48, 2.69–20.86**
Burn	100	–
Cardiovascular	95.8	0.718
Medical	98.6	0.009, 8.03, 1.1–58.74
Neurosurgery	97.1	0.358
Trauma	97.1	0.240
Visceral–thoracic	100	–

OR, odds ratio; CI, confidence interval.

Discussion

Summary of main findings

This is the first study exploring delirium at the end of life, the interrelationship of delirium and dying or terminal delirium. Notably, mortality rates were low — with defined outliers — on most services. The mortality rate was highest in the palliative care services followed by the ICUs. Conversely, the lowest mortality rates were noted on the surgical services. Similarly, the mortality risk was increased by factors 6 and 2.4 in the ICUs and medical services, respectively. Although the mortality rate varied substantially, the rates of delirium at the end of life did not: on the medical services, terminal delirium ranged from 63.2% to 100%, on the surgical services from 66.7% to 100%, and on the intermediate and intensive care services from 95.2% to 100%. Not surprisingly, with this small range, intergroup differences were barely existent. On all medical services, the risk of terminal delirium was actually reduced by two thirds and — at the opposite end — increased eightfold on the ICUs. In particular, on oncology, pulmonology, and cardiology services, this effect was noted vs. the medical regular and intensive care services.

Comparison to the existing literature

This study addresses two understudied topics: mortality rates and prevalence of terminal delirium.

Generally, mortality rates have been decreasing (Hall et al., 2013) and most patients (75%) deceasing in the hospital were >65 years of age. By first-listed diagnoses, patients died of respiratory failure 16.5%, septicemia 16.3%, chronic obstructive pulmonary disease 14.4% (Sanclemente et al., 2004), pneumonitis 13.6%, and stroke 4.7–24% (Sanclemente et al., 2004; Alvarez, 2008); to a lesser degree of acute myocardial infarction 6.7–

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8.5% (Bertomeu et al., 2013), severe hemoptysis (6.5%) (Fartoukh et al., 2012), kidney disease 3.5%, cancer 4.4%, community-acquired pneumonia 8.1% (Marrie and Wu, 2005) or general pneumonia 3.3–9.6% (Sanclemente et al., 2004), and heart disease 3.1% (Hall et al., 2013). As a limitation, only first-listed diagnoses were considered and service-related mortality was not described. For the surgical services, mortality rates were 2–6.9% (Ghaferi et al., 2009; Shidara et al., 2016), reached 5.1% for medical services (Sanclemente et al., 2004), and 56% for palliative care services (Agar et al., 2016). Thus, with respect to mortality rates, most evidence focuses on specific conditions, whereas fewer studies focus on surgical and medical services in general, and very few on palliative care.

In this comprehensive sample, mortality rates were determined across services and specific services. In general, rates were lower than in these previous reports. For the surgical services, mortality was 0.7% vs. 2–6.9% — however, services with minor surgeries, i.e., dermatology or otorhinolaryngology were included; for the medical services, rates were 4.4% vs. 5.1%, and for the ICUs 10.8%.

In addition, the odds for mortality in these services was determined and reflected the aforementioned rates: surgical OR 0.13, medical OR 1.39, and the ICUs OR 5.97. Compared with previously reported rates, the mortality was about half in palliative care (27.3% vs. up to 56%), and marginally lower in stroke patients (3.8 vs. 4.7%). In addition, mortality rates for 34 further services were determined (Table 1). In particular, those for the ICUs with increased rates and odds for delirium in the critically ill (10.8%, OR 5.97) are of interest (Klein Klouwenberg et al., 2014).

The literature determining prevalence of terminal delirium is scarce and limited to the palliative care setting, in which up to 92% of patients experience delirium at the end of life (Lawlor et al., 2000; Weckmann et al., 2014; Maldonado, 2017; Watt et al., 2019). In this study, this rate matched with 91.3%. In addition, this study was able to show that in the medical services — in particular oncology, pulmonology, and cardiology vs. internal medicine — rates for delirium at the end of life were lower, whereas on the ICUs, rates were increased; however, all of these rates were substantial. For the surgical, intermediate, and specific intensive care services, the overall and individual rates of terminal delirium also failed to separate from the general rate despite substantial variance — 66.7–100%. Thus, for these services, rates of terminal delirium were the same.

Interestingly, within the medical services, rates were lower across services and in particular, in oncology, pulmonology, and cardiology, whereas in general, medicine rates were increased. For oncological patients, a possible explanation is the curative approach followed and patients with terminal illness were likely cared for on the palliative care service. For general medicine patients, with increased rates and odds (95.8%, OR 4.12), a potential explanation would be multimorbidity, which has been associated with delirium and mortality (Grover and Avasthi, 2018).

Eventually, it is not surprising that the previously documented rate of terminal delirium in palliative care patients extends to virtually all medical fields. The end of life — dying — is commonly associated with severity of illness and multiorgan failure and once systems fail, brain function is compromised equivalent to acute brain failure, delirium (Maldonado, 2017). Thus, delirium might be considered a harbinger of death, equivalent to mental status change in the quick sepsis-related organ failure assessment score (q sofa) suggesting high risk of poor outcome in patients with suspected infection and sepsis (Siddiqui et al., 2017).

Rates of terminal delirium were the same across surgical and within surgical services, as well as for the intermediate care services. And on the ICUs, similar to the increased mortality rates, terminal delirium may have also been associated with severity of illness in the critically ill.

Implications

This study showed a strong interrelationship of delirium and death, delirium at the end of life, or terminal delirium, so delirium and death may commonly coincide. Previously only known in the palliative care setting, this interrelationship virtually extends to all medical fields.

Strengths and limitations

This study has several strengths and few limitations. First, a large sample including all eligible patients across all departments over 1 year was used avoiding bias toward specific patient groups like elderly individuals. Second, it was possible to comprehensively describe these patients with respect to their socio-demographic and medical characteristics. However, since mortality was infrequent, the numbers deteriorated within services. On the downside, the patients' population was representative of a tertiary care center and the generalizability to other settings remains to be studied. Further, it was not possible to account for the severity of illness. Nonetheless, these findings help to elucidate the extent of delirium at the end of life in various services.

Conclusion

In summary, delirium and death are strongly inter-related, so delirium might be a harbinger of death. Although the overall in-hospital mortality was low, delirium at the end of life or terminal delirium was virtually omnipresent. The implications of terminal delirium merit further studies, in particular with regard to the associated distress in patients, family members and hospital staff.

Conflicts of interest. The authors have no conflicts of interest.

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