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ORIGINAL ARTICLE

Quality of care in hospitalized cancer patients before and after implementation of a systematic prevention program for delirium: the DELTA exploratory trial

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Abstract

Background We evaluated whether the DELirium Team Approach (DELTA) program—a systematic management program aimed at screening high-risk groups and preventing delirium—would improve quality of care in patients hospitalized with cancer.

Methods A retrospective before–after study was conducted during a pre-intervention period (between October 2012 and March 2013) and a post-intervention period (between October 2013 and March 2014) at a Japanese hospital providing specialized treatments for cancer. A total of 4180 inpatients were evaluated before the implementation of the DELTA program and 3797 inpatients were evaluated after implementation.

Results After program implementation, the incidence of delirium decreased from 7.1 to 4.3% (odds ratio [OR], 0.52; 95% CI, 0.42–0.64). The incidence of adverse events, including falls or self-extubation, also decreased, from 3.5 to 2.6% (OR, 0.71; 95% CI, 0.54–0.92). There was a significant decrease in the prescription of benzodiazepines (OR, 0.79; 95% CI, 0.71–0.87), increase in the level of independence in activities of daily living at discharge (OR, 1.94; 95% CI, 1.11–3.38), and decrease in the length of stay (risk ratio 0.90; 95% CI, 0.90–0.90).

Conclusions The systematic management program for delirium decreased the incidence of delirium and improved several clinical outcomes. These data suggest that this simple cost-effective program is feasible and implementable as routine care in busy wards.

Keywords Cancer · Cognitive impairment · Delirium · Education program · Prevention

Introduction

Delirium is an acute confusional state marked by disturbance of attention, awareness, and general cognition. It can occur anywhere along the illness trajectory of patients with cancer, occurring in 13 to 42% at admission, in 14 to 60% of postoperative patients, in 18 to 56% of elderly inpatients, and up to 90% of critically ill patients in the last hours and days of the illness [6, 17, 29]. Despite the high prevalence of, and costs associated with, delirium, it is commonly underdiagnosed and untreated [39].

Delirium has short- and long-term serious outcomes. It is an independent risk factor for post-discharge mortality [34]. In

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addition, delirium increases the risk of falls [26], postoperative complications [33], non-adherence to treatment (such as pulling out of infusion lines) [8], and functional decline, and it prolongs the duration of hospital stay [19, 28] and increases the risk of institutionalization [45].

Delirium can be caused by multiple factors such as dehydration, infection, and electrolyte abnormalities, as well as by medications. Of the potentially modifiable risk factors, exposure to benzodiazepines appears to be the most strongly associated with delirium [40, 44]. Previous studies have shown that avoidance of benzodiazepines as part of a multicomponent intervention during the peri-operative period is associated with reduced risk of delirium [13] and that the use of benzodiazepines to treat delirium does not ameliorate the condition's severity [5].

As there is a little evidence supporting the efficacy of pharmacologic prevention of delirium, a great deal of attention has been devoted to non-pharmacological interventions [11, 12, 14, 15, 24, 27, 38]. Overall, these studies have shown that multicomponent interventions addressing potentially modifiable risk factors for delirium may reduce the prevalence, incidence, and duration of the condition [20, 37]. Additionally, interventions toward delirium prevention are related to improving quality of care for older people; interventions include enhanced educational approaches to develop the capacity for assessing and identifying delirium symptoms from the changes in patients' behavior and to promote practical change (application of knowledge) [7, 36, 41, 42]. Notably, at least 30 to 40% of delirium cases are considered preventable by multicomponent interventions [1, 23, 32]. In contrast to studies of the evolution of delirium prevention in non-cancer settings, studies of delirium prevention in cancer settings are still limited [10, 16, 25], and few studies have obtained positive results. For example, Hempenius et al. evaluated the efficacy of a geriatric liaison intervention in reducing the incidence of delirium after surgery for solid tumors; however, they had negative results [16]. Studies are needed to evaluate the effectiveness of multicomponent interventions for delirium prevention in diverse cancer populations in real-world practice settings.

Here, we aimed to address this gap by evaluating whether the DELirium Team Approach (DELTA) program—a systematic management program aimed at screening for high-risk groups and preventing delirium—would improve the quality of care of patients hospitalized with cancer.

Materials and methods

Study design and setting

We conducted a retrospective cohort study using a before–after approach to evaluate the effectiveness of the DELTA program. We defined two study phases: 6 months before (between October 2012 and March 2013) and 6 months after (between October 2013 and March 2014) the implementation of the DELTA program. All inpatients admitted to the National Cancer Center Hospital East over the two phases were eligible to be included in the study if they (1) were reimbursed by public health insurance; (2) were not admitted to a palliative care ward; (3) were alive at least 24 h after admission; and (4) were assessed by using the Barthel index at admission [31]. The hospital is located in Kashiwa city, Japan. It has nine general wards and an intensive care unit (400 beds), consists of 28 clinical departments (10 departments in surgery and 8 departments in medical oncology), and it provides specialized treatments for cancer. There are 118 staff doctors, 91 resident doctors, and 515 nurses in this hospital. The number of new patients is more than 7000: the number of average patients in hospital stays was 388.9/day, the number of average admissions was 46.0/day, and the number of outpatients was 1070/day in 2015. The institutional review board at the hospital approved the study protocol and waived the requirement for informed consent because the study involved retrospective chart reviews.

Delirium prevention and management program

On the basis of a focus group interview and preliminary educational workshop, we developed a delirium prevention program (DELTA program) with six components (Table 1): (1) education, (2) screening, (3) planning, (4) prevention, (5) scheduled assessment, and (6) management and treatment.

The first component was an educational package for nurses, physicians, and pharmacists. The educational package consisted of three elements (Table 1). First, all nurses working in the wards received a 90-min training session in group format about the prevention, screening, and treatment of delirium; the training was set up by experienced consultation-liaison psychiatrists. Training in delirium screening and assessment was an essential part of the session and was conducted with the aid of video-recording equipment and role-playing exercises. The lecture included basic information on delirium (definition, signs, epidemiology, and risk factors) and provided information on how to prevent delirium (by addressing potentially modifiable risk factors) and how to manage patients with delirium (by strategies such as monitoring, early detection, non-pharmacological management, and pharmacological management). After this lecture, nursing staff were divided into small groups, each consisting of three nurses and a facilitator, for role-playing and discussion. During the role-playing and discussion, the nurses were required to consider the signs of delirium, potential risk factors, and potential management for these factors. Second, physicians and

Table 1 Components of the DELTA program

Components
1. Educational package for nurses, physicians, and pharmacists.
90-min training session for nurses on prevention, screening, and treatment of delirium
30-min lecture for physicians and pharmacists on prevention and treatment of delirium
Monthly case conferences for nurses
2. Routine screening of patients at high risk for delirium
Nurses assess all patients on admission
Nurses share information with physicians
3. Planning of delirium prevention in patients at risk for delirium
Avoid polypharmacy, especially benzodiazepines, for insomnia and delirium treatment.
Prescribe atypical neuroleptics as first-line rescue medication in case of delirium.
4. Interdisciplinary approach
Promote pain control
Normalize nutrition, electrolytes, and fluid balance
Avoid constipation
Avoid infection
Promote ambulation.
5. Scheduled assessment of delirium signs by ward nurses
Use the Confusion Assessment Method every week and 1, 3, and 5 days after surgery
6. Delirium management and treatment
Administer prescribed rescue medication upon observation of early delirium symptoms
Discuss further treatment with physicians

pharmacists received a 30-min lecture on the prevention and treatment of delirium. The lecture emphasized the importance of sharing information on the risks and signs of delirium. Third, once a month, the consultation-liaison team held case conferences to boost the ability of nurses to prevent and treat patients with delirium.

The second component was routine screening for patients at risk for delirium. Nurses assessed all patients on admission and on change of the medical wards to determine whether they had risk factors for delirium, including age ≥ 70 years, dementia, alcohol consumption habit, history of delirium, and use of benzodiazepines. When a patient had one or more of these risk factors, the nurses were requested to share this information with physicians by phone and medical chart in an effort to prevent delirium. In addition, the nurses provided the information about the management of delirium to the families of the patient with risk factors.

The third component was planning of delirium prevention in patients at high risk of the condition. For those patients whom the screening revealed to be at high risk, physicians were encouraged to conduct a medication review to prevent unnecessary polypharmacy and to avoid the prescription of benzodiazepines for sleep.

The fourth component was an interdisciplinary approach. A priority list of evidence-based interdisciplinary measures to prevent and treat delirium in at-risk patients was provided to staff. Information on the list, such as pain management, normalization of fluid balance, administration of oxygen, elimination of unnecessary medications, and early mobilization, were based on the guidelines [9].

The fifth component was a scheduled (admission and every week in all wards and 1, 3, and 5 days after procedure in surgical wards) assessment of delirium signs. Nurses used the Confusion Assessment Method (Inouye, Ann Intern Med 1990) to assess whether patients at high risk of delirium had signs of the condition. The assessments were continued until the patients were discharged.

The sixth component was delirium management. Physicians were encouraged to prescribe atypical antipsychotics, when needed, for patients with delirium. In addition, interdisciplinary intervention continued to be implemented, as described in the fourth component.

The staff education was implemented in the awards of the hospital in a stepwise manner with the aid of the office of safety management. All nursing staffs took part in this program by award, the staff doctors and residents by each department. The sessions for nurses were conducted by the three

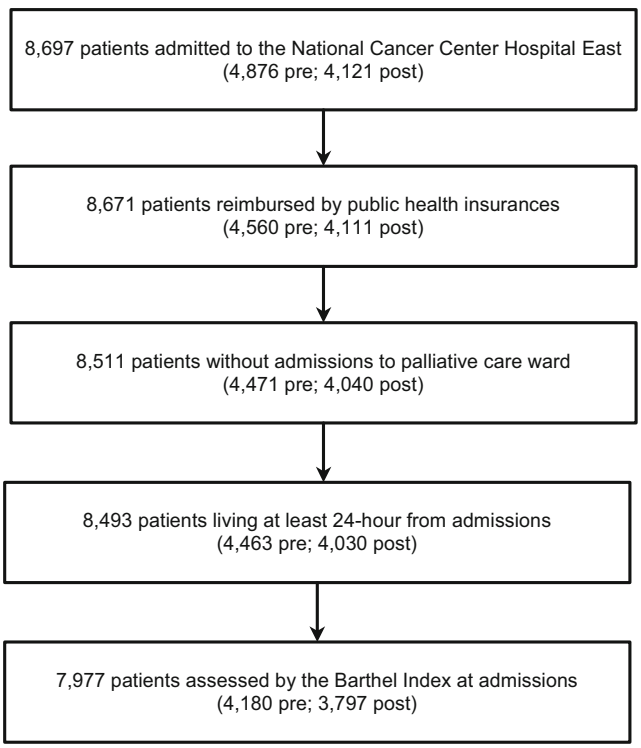

Fig. 1 Study flow diagram. The study period was divided into pre-intervention (between October 2012 and March 2013) and post-intervention (between October 2013 and March 2014)

Table 2 Demographic characteristics of pre- and post-intervention groups

	Pre-intervention ($n = 4180$)		Post-intervention ($n = 3797$)		Standardized difference (%)
	n	%	*n*	%	
Female	1312	31.4	1175	30.9	1.0
Age group (years)					
0–49	399	9.5	369	9.7	0.6
50–64	1342	32.1	1136	29.9	4.7
65–74	1690	40.4	1677	44.2	7.6
≥ 75	749	17.9	615	16.2	4.6
Diagnosis (DPC code)					
Lung cancer (040040)	856	20.5	780	20.5	0.2
Gastric cancer (060020)	519	12.4	471	12.4	0.0
Esophagus cancer (060010)	493	11.8	428	11.3	1.6
Head and neck cancer (03001x)	339	8.1	298	7.8	1.0
Hepatic cancer (060050)	292	7.0	234	6.2	3.3
Splenic tumor (06007x)	225	5.4	189	5.0	1.8
Rectal cancer (060040)	166	4.0	185	4.9	4.4
Other	1290	30.9	1212	31.9	2.3
The Charlson index					
0–1	170	4.1	108	2.8	6.7
2–3	3726	89.1	2985	78.6	28.9
≥ 4	284	6.8	704	18.5	35.9
Activities of daily living[a]					
Total to severe dependence (0–60)	137	3.3	100	2.6	3.8
Moderate to slight dependence (61–99)	275	6.6	219	5.8	3.4
Independence (100)	3768	90.1	3478	91.6	5.1
Disturbance of consciousness[b]	34	0.8	60	1.6	7.1
Surgery	2016	48.2	1704	44.9	6.7

[a] Assessed by using the Barthel Index score at admission

[b] Assessed by using the Japan Coma Scale at admission

consultation psychiatrists, one certified nurse specialist, and two clinical psychologists.

Outcomes

To assess the effectiveness of the DELTA program, we linked claims data and medical charts. Outcomes were (1) incidence of delirium, (2) delirium-free days per length of stay, (3) incidence of adverse events, including falls and self-extubation, (4) use of benzodiazepine receptor agonists (benzodiazepines), (5) benzodiazepine-free days per length of stay, (6) use of antipsychotics, (7) antipsychotic-free days per length of stay, (8) use of opioids, (9) opioid-free days per length of stay, (10) use of psychiatric consultation-liaison service, (11) activities of daily living as assessed by using the Barthel index at discharge [31], (12) discharge status, (13) length of stay, and (14) costs, including all procedural and pharmacy costs. To identify delirium, we used a standardized chart-based method, with a sensitivity of 74% and a specificity of 83% in older hospitalized patients [21]. Unit costs were converted into US dollars by using purchasing power parity (US$1.00 = JPN\103).

Statistical analyses

Clinical characteristics were compared among patients admitted during the pre-intervention period and those admitted during the post-intervention period. We used the standardized difference for categorical variables to measure covariate balance, whereby the standardized difference of > 10% represents imbalance [2]. Clinical characteristics included sex, age group, primary diagnosis, the Charlson comorbidity index [43], activities of daily living as assessed by using the Barthel index at admission, disturbance of consciousness as defined by a Japan Coma Scale score of ≥ 1 at admission [35], and surgery (Table 1). To evaluate differences in outcomes, we used logistic regression models for binomial

Table 3 Changes in outcomes after implementation of the DELTA program

Outcome	Pre-intervention ($n = 4180$)	Post-intervention ($n = 3797$)	Adjusted relative effect[e] (95% CI)
Efficacy outcomes			
Incidence of delirium[a] (%)	7.1	4.3	0.52 (0.42–0.64)*
Delirium-free days[b] (%)	97.8	98.5	1.02 (1.01–1.03)*
Safety outcome			
Falls or self-extubation[a] (%)	3.4	2.6	0.71 (0.54–0.92)*
Falls[a] (%)	2.0	1.7	0.77 (0.55–1.09)
Self-extubation[a] (%)	1.6	1.1	0.71 (0.47–1.05)
Procedural outcomes			
Prescription of benzodiazepines[a] (%)	28.8	24.0	0.79 (0.71–0.87)*
Benzodiazepine-free days[b] (%)	86.9	90.6	1.03 (1.02–1.04)*
Prescription of antipsychotics[a] (%)	15.2	20.8	1.50 (1.33–1.69)*
Antipsychotic-free days[b], %	94.7	92.6	0.98 (0.97–1.00)*
Prescription of opioids[a] (%)	22.9	22.8	1.04 (0.92–1.17)
Opioid-free days[b] (%)	95.7	95.4	1.00 (0.99–1.01)
Liaison-consultation[a] (%)	4.8	5.4	1.05 (0.85–1.30)
Outcome at discharge			
Activities of daily living[c] (%)			
Total to severe dependence (0–60)	1.6	0.9	Reference
Moderate to slight dependence (61–99)	5.4	3.2	0.94 (0.53–1.67)*
Independence (100)	93.0	95.9	1.94 (1.11–3.38)*
Discharge status[c] (%)			
Outpatient	94.5	94.8	Reference
Transportation/ nursing home	2.3	2.0	0.84 (0.61–1.16)
Death	2.5	2.5	1.03 (0.75–1.42)
Other	0.7	0.7	0.95 (0.54–1.65)
Length of stay[d], median (days) (IQR)	10 (7–16)	10 (7–15)	0.95 (0.94–0.96)*
Cost[d], median $US (IQR)	5320 (3053–10,928)	5108 (2969–9744)	0.90 (0.90–0.90)*

[a] Logistic regression model was used for binary data

[b] The Poisson regression model with offset term was used for days per length of stay

[c] Multinomial regression model was used for multinomial data

[d] The Poisson regression model was used for count data

[e] Adjusted for sex, age group, diagnosis, the Charlson index, disturbance of consciousness, level of activities of daily living, and surgery

*$P < 0.05$

outcomes (e.g., incidence of delirium), the Poisson regression models with an offset term for rates per length of stay (e.g., delirium-free days per length of stay), multinomial logistic regression models for multinomial outcomes (e.g., discharge status), and the Poisson regression models for count outcomes (e.g., costs) [30]. The models contained the main effect of study period (before vs. after implementation of the DELTA program) and the covariates listed in Table 1. These variables were entered simultaneously into the models. We estimated relative effect measures such as odds ratios (ORs) and relative risks (RRs) with their 95% confidence intervals (CIs). All analyses were performed with R version 3.2.2. For all analyses, the null hypothesis was evaluated at a two-sided significance level of 0.05.

Results

Of the 8697 potentially eligible patients, we identified a total of 7977 who met our eligibility criteria (Fig. 1). Our final analytic

Table 4 Change in outcomes after implementation by surgery

Outcome	Surgery			Without surgery		
	Pre ($n = 2016$)	Post ($n = 1704$)	Odds ratio[e] (95% CI)	Pre ($n = 2164$)	Post ($n = 2093$)	Odds ratio[e] (95% CI)
Efficacy outcomes						
Incidence of delirium[a] (%)	8.5	5.0	0.50 (0.38–0.67)*	5.9	3.7	0.55 (0.40–0.76)*
Delirium-free days[b] (%)	97.6	98.4	1.02 (1.01–1.04)*	97.9	98.5	1.01 (1.00–1.03)
Falls or self-extubation[a] (%)	4.2	2.9	0.63 (0.43–0.91)*	2.7	2.3	0.83 (0.55–1.25)
Falls[a] (%)	2.1	1.3	0.55 (0.32–0.93)*	1.8	2.0	1.00 (0.63–1.59)
Self-extubation[a] (%)	2.3	1.8	0.78 (0.48–1.25)	0.9	0.5	0.60 (0.27–1.28)
Procedural outcomes						
Prescription of benzodiazepines [a] (%)	36.6	32.9	0.82 (0.71–0.94)*	21.5	16.7	0.73 (0.62–0.86)*
Benzodiazepine-free days[b] (%)	84.8	88.1	1.03 (1.01–1.05)*	88.9	92.7	1.03 (1.01–1.05)*
Prescription of antipsychotics[a] (%)	18.9	25.5	1.50 (1.27–1.77)*	11.8	17.0	1.52 (1.26–1.83)*
Antipsychotic-free days[b] (%)	94.3	92.4	0.99 (0.97–1.00)	95.0	92.7	0.98 (0.96–1.00)*
Use of opioid[a] (%)	54.8	53.8	0.93 (0.81–1.07)	16.2	17.9	1.14 (0.96–1.36)
Opioid-free days[b] (%)	91.9	91.4	1.00 (0.98–1.01)	91.9	90.5	0.98 (0.97–1.00)
Liaison-consultation[a] (%)	5.7	5.9	0.95 (0.71–1.27)	4.0	5.0	1.19 (0.87–1.63)
Outcome at discharge						
Activity of daily living[c] (%)						
0–60	1.2	0.6	0.38 (0.14–1.04)	1.9	1.2	0.67 (0.33–1.35)
61–99	4.5	2.7	0.45 (0.29–0.69)*	6.2	3.5	0.52 (0.36–0.75)*
100	94.3	96.7	Reference	91.8	95.3	Reference
Discharge[c] (%)						
Outpatients	96.6	97.2	Reference	92.7	92.7	Reference
Transportation/nursing home	1.8	1.4	0.69 (0.40–1.21)	2.8	2.4	0.97 (0.65–1.46)
Dead	0.9	1.0	0.98 (0.48–2.00)	3.9	3.8	1.06 (0.73–1.53)
Others	0.7	0.4	0.39 (0.14–1.07)	0.6	1.1	1.69 (0.82–3.50)
Length of stay[d], mean day	15.7	15.3	0.95 (0.94–0.97)*	13.2	12.5	0.94 (0.92–0.96)*
Costs[d], mean $US (IQR)	11,568.5	11,195.3	0.95 (0.95–0.95)*	5891.2	4790.6	0.81 (0.81–0.81)*

[a] Logistic regression model was used for binary data

[b] The Poisson regression model with offset term was used for days per length of stay

[c] Multinomial regression model was used for multinomial data

[d] Poisson regression model was used for count data

[e] Adjusted for sex, age group, diagnosis, the Charlson index, disturbed consciousness, and activity of daily living

*$P < 0.05$

sample totaled 4180 patients in the pre-intervention period and 3797 in the post-intervention period. Patients in the pre- and post-intervention periods differed meaningfully only in terms of the Charlson comorbidity index (Table 2). In the post-intervention period, 5061 assessments for risk of delirium were performed and the 2621 patients were considered to be at risk of delirium.

We used regression models to obtain adjusted relative effect measures for outcomes (Table 3). After the implementation of the DELTA program, the incidence of delirium decreased from 7.1 to 4.3% (odds ratio (OR), 0.52; 95% CI, 0.42–0.64). There was a 2% increase in the number of delirium-free days per length of stay (RR, 1.02; 95% CI, 1.01–1.03).

The incidence of adverse events, namely falls or self-extubation, decreased from 3.5 to 2.6% (OR, 0.71; 95% CI, 0.54–0.92). The direction of this effect was the same as for each individual component, although the estimates were unstable because of small event sizes.

The DELTA program produced significant changes in prescribing practices. The proportion of patients with prescriptions for benzodiazepines decreased from 28.8 to 24.0% (OR, 0.79; 95% CI, 0.71–0.87). Among benzodiazepines, prescription of zopiclone decreased markedly from 15.0 to 9.4%. However, the proportion of patients with prescriptions for antipsychotics increased from 15.2 to 20.8% (OR, 1.50; 95% CI 1.33, 1.69). Among antipsychotics, prescription of quetiapine markedly increased from 6.5 to 10.4%.

The DELTA program improved several clinical outcomes at discharge. The odds of independence in activities of daily living at discharge increased significantly from the pre-intervention period to the post-intervention period (93.0 vs. 95.9%; OR, 1.94; 95% CI, 1.11–3.38) (Table 4). The Poisson regression models showed a reduction rate of 5% in the length of stay (RR, 0.95; 95% CI, 0.94–0.96) and a cost rate reduction of 10% (RR 0.90; 95% CI, 0.90–0.90) after implementation of the DELTA program. In addition, when investigating the efficacy of the DELTA program in the different settings, this program reduced the incidence of delirium, the length of stay, and medical costs and improved the

odds of independence in activity of daily living at discharge in both surgical and non- surgical setting, which, on the other hand, decreased the incidence of falls or self-extubation only in a surgical setting.

Discussion

To our knowledge, this is the first study to demonstrate the effectiveness of a multicomponent intervention for delirium prevention in patients hospitalized with cancer in a real-world practice setting. Implementation of the DELTA program was associated with a 48% reduction in delirium incidence (from 7.1 to 4.3%). Our novel and important finding was that falls and self-extubation also decreased, from 3.5 to 2.6% (a 29% reduction) after implementation of the DELTA program. Although general hospitals prioritize efforts for preventing falls and pulling out of infusion lines—and delirium is the leading cause of these events—most fall interventions to date have focused on identifying fall risks and implementing various alarms that limit patient mobility [3, 18]. However, these approaches can result in unintended consequences, including physical and cognitive decline, and a strategy for fall prevention in acute care settings is still not established [22].

Second, we observed a change in the prescribing practices of physicians. There was a significant decrease in benzodiazepine prescriptions but a significant increase in antipsychotic prescriptions. This change in prescribing practices may have contributed to an improvement in the course of delirium because of their consumption levels. In Japan, there are 33 oral benzodiazepines and benzodiazepine-related drugs approved. The consumption level for benzodiazepines expressed in defined daily dose for statistical purposes (S-DDD) was much higher in Japan (46 S-DDD/1000 inhabitants/day) than those reported in the USA (8 S-DDD/1000 inhabitants/day) and France (15 S-DDD/1000 inhabitants/day) [4]. On the other hand, the consumption level for opioids in expressed in morphine equivalents was much lower in Japan (118 g/million inhabitants/day) than those reported in the USA (1776 g/million inhabitants/day) and France (711 g/million inhabitants/day).

Third, implementation of the DELTA program was associated with an increase in the level of independence in activities of daily living at discharge and a decrease in the length of stay. These results suggest that the intervention program might aid patient recovery, which is critically important to patients and their families.

Limitations

Our study had several limitations. First, we used an observational before–after study design rather than a randomized controlled trial; therefore, unmeasured confounders may have contributed to the associations found. Second, our assessment of delirium outcome was based on the chart-review method, which might have introduced information bias. The hypoactive delirium might be underestimated and the identification of delirium at admission because information before hospitalization was not sufficient to assess the cognitive impairment. Third, the single-center nature of the study limits its generalizability. The delirium incidence in our study was lower than the previous studies. It may be due to our sample including the patients with high performance status and about 90% of the patients are independent of activities of daily living on admission. Under the condition of the higher risk group, the effects of our intervention may be understood more clearly.

Conclusions

Systematic intervention for delirium decreased the incidence of the condition and improved associated clinical outcomes. Our data suggest that this simple cost-effective program is feasible and implementable as part of routine care in busy wards. A randomized controlled trial is needed to enable us to draw more definitive conclusions regarding the efficacy of the intervention.

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Compliance with ethical standards

Research ethics and patient consent This study was conducted in accordance with the amended Declaration of Helsinki and was approved by the Ethical Committee of the National Cancer Center, Japan (2014-028, approval no.: 2014-028). The full protocol is available from the corresponding author.

Conflict of interest The authors declare that they have no conflict of interest.

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