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Demographic and clinical characteristics of patients with delirium: analysis of a nationwide Japanese medical database

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ABSTRACT

Objectives Delirium commonly occurs during hospitalisation and is associated with increased mortality, especially in elderly patients. This study aimed to determine the demographic and clinical characteristics of patients with delirium in the Japanese real-world clinical setting using a nationwide database comprising claims and discharge abstract data.

Design This was an observational, cross-sectional, retrospective study in hospitalised patients with an incident delirium identified by a diagnosis based on International Classification of Diseases, 10th Revision codes or initiating antipsychotics recommended for delirium treatment in Japan during their hospitalisation.

Setting Patients from the Medical Data Vision database including more than 400 acute care hospitals in Japan were evaluated from admission to discharge.

Participants Of the 32 910 227 patients who were included in the database between April 2012 and September 2020, a total of 145 219 patients met the criteria for delirium.

Primary and secondary outcome measures Demographic and baseline characteristics, comorbidities, clinical profiles and pharmacological treatments were evaluated in patients with delirium.

Results The mean (SD) patient age was 76.5 (13.8) years. More than half of the patients (n=82 159; 56.6%) were male. The most frequent comorbidities were circulatory system diseases, observed in 81 954 (56.4%) patients. Potentially inappropriate medications (PIMs) with risk of delirium including benzodiazepines and opioids were prescribed to 76 798 (52.9%) patients. Approximately three-fourths of these patients (56 949; 74.2%) were prescribed ≥4 PIMs. The most prescribed treatment for delirium was injectable haloperidol (n=82 490; 56.8%). Mean (SD) length of hospitalisation was 16.0 (12.1) days.

Conclusions The study results provide comprehensive details of the clinical characteristics of patients with delirium and treatment patterns with antipsychotics in the Japanese acute care setting. In this patient population, the prescription rate of injectable haloperidol and PIMs was high, suggesting the need for improved understanding among healthcare providers about the appropriate management of delirium, which may benefit patients.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This was the first nationwide study that comprehensively assessed the clinical characteristics of patients with delirium in the real-world setting of acute care hospitals in Japan.

⇒ Analysis of the nationwide claims and discharge abstract database, using an algorithm adapted to the Japanese clinical setting, enabled identification of a large sample of patients with delirium in acute care hospitals in Japan.

⇒ As data were identified from the Medical Data Vision database, which is designed to capture claims and discharge abstracts in Japan and is not for research use, misclassification of the International Classification of Diseases, 10th Revision codes may occur, given that no quality check is performed.

INTRODUCTION

Delirium is an acute condition characterised by fluctuating disturbances in attention, awareness and cognition.[1] It frequently occurs in hospitalised elderly patients in an acute care setting, especially those in intensive care units (ICUs), and in postoperative care settings.[2 3] The prevalence of delirium is reported as 10%–31% among hospitalised patients within 24 hours of admission.[4] Among elderly patients, the prevalence is reported as 15%–53% after surgery[5 6] and 80% in those admitted to the ICU.[5] Previous studies have shown that delirium is associated with prolonged hospital stay and institutionalisation[2 7] and increased mortality in non-surgical and surgical patients in general wards, emergency departments and ICUs.[7 8] Furthermore, long-term cognitive and functional decline is associated with delirium, often lasting up to a year following hospital discharge.[7 9] Consequently, delirium increases economic burden by raising healthcare expenditure and imposing costs related to loss of well-being.[3]

Despite its high prevalence and poor prognosis, delirium remains unrecognised in a substantial proportion of old patients. In a prospective clinical epidemiological study, even nursing personnel were unable to recognise delirium in up to two-thirds of the hospitalised elderly patients.[10] Recent evidence suggests that antipsychotics and multicomponent interventions can notably reduce the incidence of delirium and improve clinical outcomes,[11–13] emphasising the need for early intervention and prevention in the hospitalised or postoperative elderly population that is at risk of delirium.[14]

Antipsychotics are widely used for the treatment of delirium, although no standard clinical pathway for the management of delirium has been established. The Japanese Ministry of Health, Labour and Welfare issued a notification in 2011, permitting the reimbursement of off-label oral and injectable haloperidol, oral perospirone, quetiapine and risperidone for the treatment of delirium, psychomotor agitation and irritability associated with organic diseases.[15] In addition, the Japanese Society of General Hospital Psychiatry recommended the use of several antipsychotics in a pharmacotherapy algorithm for delirium.[16] However, few studies have quantitatively investigated the use of antipsychotics for the treatment of patients with delirium in real-world clinical practice in Japan.[17 18]

A limited number of studies have examined the characteristics of patients experiencing delirium based on a medical database.[17–25] This is because identification of delirium through a medical database is quite challenging, given the inconsistent and poor documentation of records.[26] Moreover, the identification of delirium requires bedside cognitive assessments and application of validated diagnostic tools such as the Confusion Assessment Method[27] or the Diagnostic and Statistical Manual of Mental Disorders criteria.[1] Therefore, delirium is not routinely evaluated in acute care hospitals,[26 28] and the information on delirium diagnosis rarely gets recorded in healthcare utilisation databases (eg, claims data or hospital clinical data repository).

Although several medical database studies in the USA[19] and Japan[24] have used International Classification of Diseases, 9th Revision (ICD-9) or ICD, 10th Revision (ICD-10) codes to identify patients with a diagnosis of delirium, only around 2% of patients with delirium (postoperative in Japan) could be identified. On the other hand, several medical database studies have employed antipsychotic use to identify patients with delirium.[21 23 25] However, either of these criteria, when used exclusively, may be inadequate in obtaining a comprehensive and true picture of patients with delirium in the real-world clinical setting in Japan.

To date, few studies have investigated the overall profile of patients with delirium in the real-world clinical setting in Japan. The present study aimed to assess the demographic characteristics, comorbidities, clinical profiles and treatments in patients with delirium during hospitalisation from a nationwide administrative database of acute care hospitals in Japan, the Medical Data Vision (MDV) database. In this study, delirium was defined using the algorithms that were recommended in the recently published claims-based database studies with slight modifications.[22 24]

METHODS

Study design

This was a retrospective, cross-sectional, observational study using a nationwide administrative database (MDV Co, Tokyo, Japan), with data collected from 1 April 2012 to 30 September 2020. The MDV database contains anonymised administrative data of more than 30 million patients from over 400 hospitals, which cover approximately 24% of all acute care hospitals in Japan. The MDV database includes claims data and discharge abstract data collected from inpatient and outpatient visits.

Patient selection

In this study, patients admitted to general wards and ICUs were included. Patients meeting the prespecified delirium identification algorithm criteria who were hospitalised for surgery or an emergency and those who were discharged, transferred to other hospitals or died after hospitalisation during the study period were included in the analysed data set.

The delirium identification algorithm in this study was based on that recently reported by Kim et al.[22] Kim et al proposed an algorithm that defines delirium based on ICD diagnosis codes or antipsychotic use and has a modestly better profile (30% sensitivity; 97% specificity) than existing algorithms such as either ICD diagnosis codes alone or antipsychotic use alone. In this study, patients were identified and included as the study participants based on the following criteria: a confirmed diagnosis of delirium during hospitalisation, coded as F05 per ICD-10 (criterion 1), or prescription of at least one antipsychotic agent (haloperidol, olanzapine, perospirone, quetiapine or risperidone) between the index date (admission date) and the next 7 days (criterion 2). The algorithm was modified to adjust with the clinical setting in Japan. Patients with a minimum stay of 3 days, including at least two antipsychotic-free days, were included in the study.[23] This 'two day washout' period after hospitalisation allowed the exclusion of patients who already had a prescription of the selected antipsychotic because of pre-existing conditions. Patients who were hospitalised for less than 3 days; who had schizophrenia spectrum disorder (F20–29 codes per ICD-10), bipolar disorder (F30–31 codes per ICD-10) or delirium (F05 code per ICD-10) as 'admission-precipitating diagnosis' or 'comorbidities present on admission'; who were prescribed antipsychotics on the hospitalisation date or the next day; and who were prescribed olanzapine in combination with cisplatin for nausea within 1 week from the index date were excluded from the analyses.

Patients hospitalised multiple times were evaluated only at the first hospitalisation when the inclusion criteria were met. Repeated episodes of delirium in the same patient were not tracked or included in the analysis. The observation period was from the index date (date of hospitalisation) to the end of hospitalisation, defined as discharge, hospital transfer or death of the patient.

Outcomes

The following demographic and baseline characteristics, clinical profiles and comorbidities of patients with delirium were assessed from the MDV database: patients' baseline characteristics (sex, age, activities of daily living [ADL] score calculated using the Barthel Index,[29] cognitive impairment [assessed as 'present' if the patient was previously diagnosed with dementia or prescribed antidementia medications or had a low degree of independence]), inpatient departments, comorbidities, type of clinical practice (delirium-associated PIM use [identified based on the Beers Criteria,[30] the Guidelines for Medical Treatment and its Safety in the Elderly from the Japan Geriatrics Society Working Group[31] and the report from Noshiro et al[32]], type of surgery [sites or duration of anaesthesia], duration of hospitalisation and ICU stay), hospitalisation information (type of hospitalisation [surgery or emergency hospitalisation], number of beds), prescription pattern for each antipsychotic and patient outcomes (transfer to other hospitals/nursing homes, death). Among the outcomes, age, ADL, cognitive impairment and comorbidities were assessed as the risk (predisposing) factors of delirium. Surgery information, hospitalisation information (surgery or emergency) and PIM use were assessed as triggers (precipitating factors) of delirium.[8]

Statistical analysis

The aim of this study was descriptive; therefore, no sample size calculations were performed. Data were summarised as mean (SD) or number and frequency (%). All statistical analyses were performed using SAS V.9.4 (SAS Institute).

Sensitivity analysis

As many assumptions were made while creating the delirium identification algorithm, two sensitivity analyses (SAs) were conducted for patients selected in the main analyses to confirm how different assumptions on the analysed populations might have influenced the outcomes. As some patients could have undergone surgery several days after their admission and the criteria used to identify patients to be included in the main analysis do not allow their inclusion, patients who had a prescription of any of the 'selected' antipsychotics between the third day of hospitalisation and the day of discharge (or transfer or death) were included in SA1. Furthermore, as some patients may undergo surgery immediately after the emergency admission and have delirium on the next day and the criteria set for the main analysis do not allow their inclusion, patients who had a prescription of the specified antipsychotics between the second and the eighth day of hospitalisation were included in SA2.

Patient and public involvement

Patients were not involved in any phase of this retrospective study, and data were collected from deidentified administrative claims database.

RESULTS

Identification of patients with delirium

Of the 32 910 227 patients who were included in the MDV database during the study period, 145 219 were identified
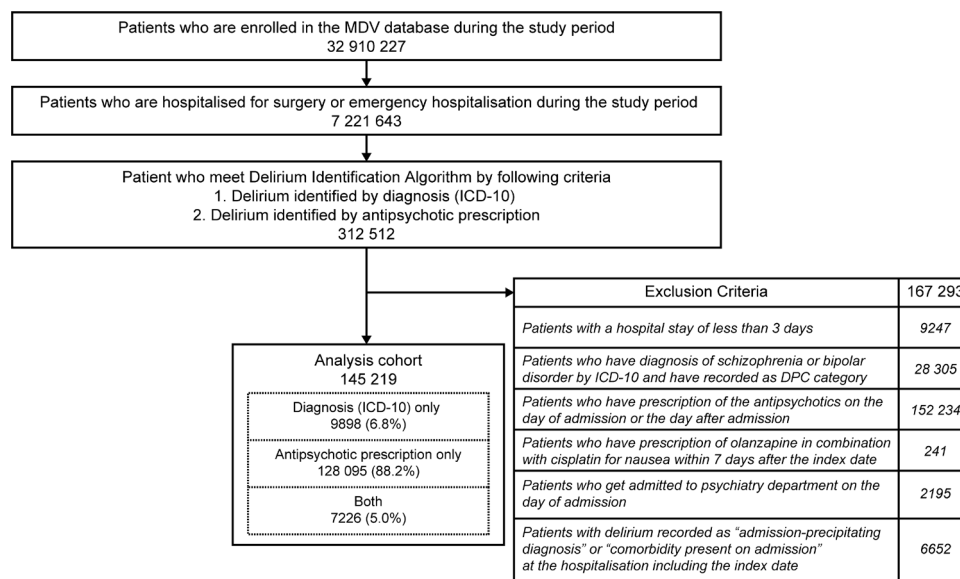

Figure 1 Patient selection flow chart. DPC, diagnosis procedure combination; ICD-10, International Classification of Diseases, 10th Revision; MDV, Medical Data Vision.

as having delirium (figure 1). Among patients who were hospitalised for surgery or an emergency (n=7 221 643), 2.0% were identified as having delirium. Overall, 9898 (6.8%) patients who met the delirium identification algorithm criteria were diagnosed with delirium based on ICD-10 codes and did not receive any of the selected antipsychotic treatments during their hospitalisation; 128 095 (88.2%) patients were identified because they had been prescribed any of the selected antipsychotics, and 7226 (5.0%) patients who met the delirium identification algorithm criteria had both a diagnosis of delirium and an antipsychotic prescription (figure 1). Most (n=14 801; 86.4%) of the 17 124 patients with an ICD-10-coded diagnosis had 'delirium' (code F05.9), followed by 'nocturnal delirium' (code F05.9), 'delirium superimposed on dementia' (code F05.1) and 'delirium not superimposed on dementia' (code F05.0; online supplemental table 1).

Patient demographics and baseline characteristics

Mean (SD) patient age was 76.5 (13.8) years, and approximately 65% of patients were ≥75 years of age; more than 50% (n=82 159) of patients were male. Approximately half (n=76 422; 52.6%) of the patients with delirium were categorised as 'dependent (need someone's help)' based on the Barthel Index score (table 1). Cognitive impairment was noted in 40 376 (27.8%) patients (table 1; online supplemental table 2). Circulatory system diseases were the most common comorbidity, observed in 81 954 (56.4%) patients, followed by endocrine, nutritional and metabolic diseases (n=59 955; 41.3%) and digestive system diseases (n=59 691; 41.1%; table 1; online supplemental table 3). These outcomes were assessed as the risk (predisposing) factors of delirium.

Clinical practice

Around half (n=85 492; 58.9%) of the patients with delirium underwent any surgery, of whom approximately one-third (n=28 557) were anaesthetised for more than 2 hours (table 2). There was a wide distribution of surgical sites, with the abdomen being the most common site (n=38 898; 26.8%; online supplemental table 4). Mean (SD) duration of hospitalisation was 16.0 (12.1) days; 55 709 (38.4%) patients were hospitalised for 1–2 weeks (table 2). Overall, 33 718 (23.2%) patients were admitted to the ICU for a mean (SD) of 3.4 (3.1) days, of whom 4379 (3.0%) spent at least 7 days in the ICU (table 2). PIMs were prescribed to 76 798 (52.9%) patients, including benzodiazepines in 31 324 (21.6%) patients and opioids in 29 268 (20.2%) patients. Approximately three-fourths (n=56 949; 74.2%) of these patients were prescribed ≥4 PIMs. Multiple classes of PIMs were used by 38.6% of patients to whom PIMs were prescribed (table 2). These factors were assessed as triggers (precipitating factors) of delirium.

Treatment for delirium

Injectable haloperidol was the most prescribed antipsychotic (n=82 490; 56.8%) for the treatment of delirium,

followed by risperidone solution (n=34 282; 23.6%), quetiapine tablet (n=19 830; 13.7%), risperidone orodispersible tablet (n=7645; 5.3%) and risperidone tablet (n=4958; 3.4%; table 3). The mean (SD) duration of these antipsychotic prescriptions was 5.4 (8.1) days (table 3).

Hospitalisations and patient outcome

Assessment of patients with delirium by hospital department showed that the departments where at least 5% of patients experienced delirium were surgery (n=28 656; 19.7%), internal medicine (n=28 232; 19.4%), gastroenterology (n=15 445; 10.6%), cardiology (n=12 337; 8.5%), orthopaedics (n=11 302; 7.8%) and neurosurgery (n=8144; 5.6%; table 1; online supplemental table 4). In general, 52 766 (36.3%) patients with delirium were hospitalised for planned elective surgery, whereas 59 727 (41.1%) patients were hospitalised due to an emergency (without subsequent surgery) and 32 726 (22.5%) patients were hospitalised due to an emergency and underwent surgery (online supplemental table 4). A total of 15 556 (10.7%) patients died while in hospital, and 22 081 (15.2%) were transferred to other hospitals or clinics (table 4).

Sensitivity analysis

The results of the SAs identified 184 817 patients with delirium in SA1 and 213 844 in SA2 (online supplemental figure 1). Patients' mean (SD) age was 76.1 (13.8) years in SA1 and 76.3 (14.1) years in SA2. A total of 96 591 (52.3%) patients in SA1 and 113 005 (52.8%) patients in SA2 were classified as dependent (online supplemental table 5).

The proportion of patients prescribed one or more antipsychotics to treat their delirium was 95.5% in SA1 and 95.4% in SA2. The proportion of injectable haloperidol prescriptions was 58.1% in SA1 and 60.1% in SA2, while the proportion of prescriptions for risperidone solution was 24.8% in SA1 and 23.5% in SA2 and that for risperidone tablets was 4.0% in SA1 and 3.5% in SA2 (online supplemental table 5).

DISCUSSION

The present study was the first nationwide database study that assessed the clinical characteristics of patients with delirium in acute care hospitals in Japan. To identify patients with delirium from the hospital database, the study used the delirium identification algorithm which consists of diagnoses based on ICD-10 codes and prescriptions of antipsychotics frequently used in the treatment of delirium.[22] The prevalence of delirium obtained in our study was 2.0% among patients who were hospitalised for surgery or an emergency, which was lower than the incidence of new delirium per admission (3%–29%) reported in a systematic review of the literature.[4] The low prevalence of delirium might be due to the sensitivity of the algorithm used in our study. A potential explanation is that physicians are not aware of delirium, thereby

Table 1 Patient demographic and baseline characteristics

		Patients, n (%)
Patients (n)		145 219
Age (years)	Mean (SD)	76.5 (13.8)
	≤64	22 168 (15.3)
	65–74	28 371 (19.5)
	75–84	49 739 (34.3)
	≥85	44 941 (30.9)
Sex	Male	82 159 (56.6)
	Female	63 060 (43.4)
ADL score (points)*	Dependent group (0–59)	76 422 (52.6)
	Independent group (60–100)	66 381 (45.7)
	Unknown	2416 (1.7)
Cognitive impairment†	Yes	40 376 (27.8)
	No	104 843 (72.2)
Inpatient department	Surgery	28 656 (19.7)
	Internal medicine	28 232 (19.4)
	Gastroenterology	15 445 (10.6)
	Cardiology	12 337 (8.5)
	Orthopaedics	11 302 (7.8)
	Neurosurgery	8144 (5.6)
	Urology	7031 (4.8)
	Cardiovascular surgery	6042 (4.2)
	Respiratory medicine	5506 (3.8)
	Gastrointestinal surgery	4093 (2.8)
	Emergency medicine	3414 (2.4)
	Neurology	3008 (2.1)
	Others	11 573 (8.0)
Comorbidities (ICD-10 major category)‡	Circulatory system diseases (I00–I99)	81 954 (56.4)
	Endocrine, nutritional and metabolic diseases (E00–E90)	59 955 (41.3)
	Digestive system diseases (K00–K93)	59 691 (41.1)
	Malignant neoplasms (C00–C97)	41 710 (28.7)
	Respiratory system diseases (J00–J99)	36 958 (25.4)

*Barthel Index was used for evaluation.
†Cognitive impairment was assessed as 'present' if the patient was previously diagnosed with dementia or prescribed antidementia drugs or had a low degree of independence.
‡Top 5 major ICD-10 categories are presented.
ADL, activities of daily living; ICD-10, International Classification of Diseases, 10th Revision.

leading to its inappropriate management. Another possible explanation is that physicians do not proactively record a diagnosis of delirium in claims because there is no approved drug for delirium treatment or prevention in Japan, except for tiapride that is approved for the management of delirium after stroke.

In our study, about half of the patients (n=85 492; 58.9%) underwent surgery during their hospital stay, and delirium was also identified among non-surgical patients in general medical wards such as internal medicine, gastroenterology and cardiology. A systematic literature review reported the prevalence of delirium among patients admitted to general medical and geriatric wards as 18%–35%.[8] Our findings revealed the occurrence of delirium in broad clinical departments in Japanese acute care hospitals, suggesting the need for physicians and nurses in these departments to understand the diagnosis and management of patients with delirium.

Drug classes such as benzodiazepines, opioids and H2 blockers were selected as PIMs, which are reported to be

Table 2 Clinical practice

		Patients, n (%)
Patients (n)		145 219
Prescription of PIM	Yes (any type of PIM)	76 798 (52.9)
	Antidepressants	299 (0.2)
	Anticholinergic drugs	163 (0.1)
	Benzodiazepines	31 324 (21.6)
	Non-benzodiazepines	10 582 (7.3)
	Corticosteroids	16 879 (11.6)
	H1 receptor antagonists	10 283 (7.1)
	H2 receptor antagonists	17 360 (12.0)
	Opioids	29 268 (20.2)
	Number of PIMs (drugs)	76 798 (100.0)
	1	5268 (6.9)
	2	7232 (9.4)
	3	7349 (9.6)
	≥4	56 949 (74.2)
	Number of PIMs (classes)	76 798 (100.0)
	1	47 128 (61.4)
	2	21 637 (28.2)
	3	6561 (8.5)
	≥4	1472 (1.9)
Surgery	Yes	85 492 (58.9)
	Anaesthesia type/duration	85 492 (100.0)
	Surgery+no anaesthesia/local anaesthesia/light general anaesthesia	35 048 (41.0)
	Surgery+general anaesthesia (<2 hours)	21 887 (25.6)
	Surgery+general anaesthesia (≥2 hours)	28 557 (33.4)
Duration of hospitalisation (days)	Mean (SD)	16.0 (12.1)
	≤1 week	22 542 (15.5)
	>1 to ≤2 weeks	55 709 (38.4)
	>2 to ≤3 weeks	38 342 (26.4)
	>3 to ≤4 weeks	17 004 (11.7)
	>4 to ≤12 weeks	11 046 (7.6)
	>12 weeks	576 (0.4)
Use of ICU	Yes	33 718 (23.2)
Duration of ICU (days)	Mean (SD)	3.4 (3.1)
	1 day	12 218 (8.4)
	2 days	5970 (4.1)
	3 days	4247 (2.9)
	4 days	3104 (2.1)
	5 days	2192 (1.5)
	6 days	1608 (1.1)
	≥7 days	4379 (3.0)

ICU, intensive care unit; PIM, potentially inappropriate medication.

Table 3 Antipsychotics used for treating delirium

			Patients, n (%)
Patients (n)			145 219
Antipsychotics used for delirium	Yes		135 321 (93.2)
Type of drug formulation	Haloperidol	INJ	82 490 (56.8)
		TAB	1913 (1.3)
		FGR	192 (0.1)
		SOL	13 (0.0)
	Risperidone	SOL	34 282 (23.6)
		ODT	7645 (5.3)
		TAB	4958 (3.4)
		FGR	257 (0.2)
		INJ	6 (0.0)
	Quetiapine	TAB	19 830 (13.7)
		FGR	652 (0.4)
		SRT	20 (0.0)
	Olanzapine	TAB	2262 (1.6)
		ODT	915 (0.6)
		FGR	156 (0.1)
		INJ	11 (0.0)
	Perospirone	TAB	2210 (1.5)
Duration of prescription (days)	Mean (SD)		5.4 (8.1)

FGR, fine granule; INJ, injectable; ODT, orodispersible tablet; SOL, solution; SRT, sustained release tablet; TAB, tablet.

Table 4 Patient outcome—transfer to other hospitals/ nursing homes and death

		Patients, n (%)
Patients (n)		145 219
Transfer to other hospitals/nursing homes	Yes	32 651 (22.5)
	Transfer to other hospitals or clinics	22 081 (15.2)
	Admission to social welfare facilities or fee-based homes for the elderly, etc	5070 (3.5)
	Admission to facilities covered by public aid providing long-term care to the elderly	3017 (2.1)
	Admission to long-term care health facilities	2472 (1.7)
	Nursing home	11 (0.0)
Death	Yes	15 556 (10.7)
	No	129 637 (89.3)

associated with the onset of delirium in guidelines[30 31] and several studies.[32–36] In our study, more than half (52.9%) of the patients were prescribed a PIM of any type; approximately one-fifth of the patients were prescribed either benzodiazepines or opioids (21.6% and 20.2%, respectively). Benzodiazepines and opioids are associated with an increased risk of delirium in medical and surgical patients.[34] In a single-centre study in Canada, the risk was more than doubled within 28 days of hospitalisation in patients with cancer who were receiving benzodiazepines (>2 mg/day) and opioids (>90 mg/day).[37] It should be noted that Japan is one of the countries with a high rate of consumption of benzodiazepine-type sedative hypnotics.[38] In addition, opioids are necessary to control severe pain, and pain is also known to be associated with a risk of delirium,[16] suggesting the importance of delirium control in combination with pain control. PIMs also include several drugs with anticholinergic activities, such as antihistamines and antidepressants.[30] Use of anticholinergic drugs is associated with an increased risk of delirium.[39 40] Thus, physicians should avoid unnecessarily prescribing drugs with anticholinergic effects considering the risk of delirium onset. Furthermore, at least four PIMs were prescribed in 74.2% of patients with delirium in the present study. Polypharmacy with ≥3 drugs is reported to increase the risk of delirium by 2.9

times in elderly patients during hospitalisation.[41] As drug interactions are a concern regarding PIMs in patients with polypharmacy, potential drug interactions in addition to the number of PIMs used should be carefully considered especially in patients with polypharmacy. The frequent use of PIMs that increase the risk of delirium in the real world, particularly in elderly patients, reaffirms the need for a better understanding of the benefit-risk profile of such medications.

In our study, injectable haloperidol was the most frequently prescribed (56.8%) antipsychotic, followed by risperidone solution (23.6%) and quetiapine tablets (13.7%) in patients with delirium. The outcomes are similar to those from a recent database study in Japan, where haloperidol infusion was the most frequently used treatment in postoperative patients with delirium.[17] These results are also consistent with those of a questionnaire-based cross-sectional study in which more than two-thirds of Japanese experts recommended intravenous haloperidol as the initial drug (if an intravenous line was placed during hospitalisation) and atypical oral antipsychotics such as risperidone or quetiapine as initial oral drugs for hyperactive delirium.[42] Risperidone solution and olanzapine orodispersible tablets could be useful for patients who have difficulties in taking medicines.[16] In our study, a relatively high proportion of patients were prescribed risperidone solution (23.6%); however, only 0.6% were prescribed olanzapine orodispersible tablets. The low proportion of olanzapine prescription could be due to the long half-life of olanzapine and its contraindication in patients with diabetes in Japan.[16] Overall, our findings suggest that injectable haloperidol is the major treatment modality for delirium in an acute care setting likely because it can be used as needed for the treatment of delirium in such a setting. Unlike psychiatrists, the majority of physicians who treat patients with delirium are likely to be unfamiliar with use of atypical antipsychotics. However, in a broader clinical context, the risk of death in the elderly was reported to be 2.26-fold higher with haloperidol versus olanzapine,[43] and the likelihood of overall survival was 1.73-fold higher with placebo in a randomised controlled trial.[44] Moreover, the incidence of adverse events, particularly extrapyramidal symptoms, is reportedly higher with haloperidol versus risperidone, although their efficacy is reportedly similar.[45 46] While antipsychotics are frequently used for treating delirium in real-world clinical settings, physicians should note that non-pharmacological treatment is the first-line therapy for delirium and that antipsychotic use should be considered only if the non-pharmacological treatment is ineffective and patients are at risk of injuring themselves and others. For example, the National Institute for Health and Care Excellence delirium guidelines state that short-term haloperidol may be given when an individual with delirium is distressed or considered to be at risk to themselves or others and if verbal and non-verbal de-escalation methods have not shown effect.[47] The Beers Criteria by the American Geriatrics Society recommend that PIMs

including antipsychotics be avoided in older adults at high risk of delirium owing to the risk of inducing or worsening the condition.[30] Moreover, olanzapine has anticholinergic effects, and its use in managing delirium is controversial because some case reports have shown that its use may be associated with delirium onset.[48 49] Therefore, it is important for healthcare providers to understand the appropriate non-pharmacological management of delirium.

The greatest strength of this study is the large size of the MDV database, which enabled the identification of a large number of patients with delirium. The use of our algorithm optimised for the Japanese clinical setting led to an increased number of patients being retrieved from hospital databases, thus highlighting the utility of this algorithm in real-world scenarios. More importantly, outcomes of the SAs, which considered different treatment time frames in determining index, were consistent with those of the main analysis, reinforcing the robustness of our study results. The prevalence of delirium obtained by identifying patients using an ICD-coded diagnosis was only 0.2% among patients who were hospitalised for surgery or an emergency in our study, which is similar to that reported in previous studies in Japan.[18 24] However, this low prevalence may not be a true reflection of the occurrence of delirium in the real world, as observed in a prospective study that compared the sensitivity and specificity of various delirium identification algorithms.[22] According to Sakakibara et al, delirium is recorded on the claims receipt only for patients with severe delirium requiring more medical resources, but not for those with mild-to-moderate delirium.[24] Our results confirm that the majority of Japanese patients with delirium can be identified from a Japanese claims database based on prescription of an antipsychotic during their hospital stay; 88.2% of patients with delirium were identified based on an antipsychotic prescription. A recent study employing a Japanese national inpatient database used the daily nursing necessity score (dangerous behaviour or misunderstanding of nursing instructions) as the criterion of delirium, but reported a prevalence of delirium of approximately 1% (n=21 182) among 2 070 000 postoperative patients.[17] The results of the present study show the feasibility of using administrative databases for identifying patients with delirium in an acute care hospital setting in Japan.

This study has several limitations. First, the data were extracted from the MDV database, which is designed primarily for insurance purposes and not for research; therefore, no quality checks for data are performed and there is a likelihood of misclassification of ICD-10 coding. Second, as the data of patients transferred to other hospitals were not registered in this database, patients who were moved to or hospitalised in a different hospital after the index hospitalisation could not be identified. This could have led to multiple hospitalisations of the same high-risk patients, with multiple episodes of delirium at different times being identified as separate events and

possibly increasing the number of identified cases. Third, the number of prescribed antipsychotics may be inflated because some patients with psychotic disorders may have been included from the database during analysis although the present study excluded patients with schizophrenia or bipolar disease. Lastly, the sensitivity and specificity of the modified delirium identification algorithm used in this study have not yet been validated in Japan. The recent addition of a medical fee for the care of high-risk patients with delirium in the medical reimbursement revision of 2020 in Japan may increase the accuracy of identification of patients with delirium from the medical database. For future research, the delirium identification algorithm used in our study needs to be validated.

In conclusion, the results of the present study provide comprehensive details of the clinical characteristics of patients with delirium and treatment patterns with antipsychotics in the Japanese acute care setting. The results reinforce the need to consider the risk of delirium in hospitals, especially in high-risk patients, and provide useful information for healthcare professionals to understand the clinical profile of patients who are likely to experience delirium when hospitalised. The study reveals two important findings in this patient population: (1) the high prescription rate of injectable haloperidol and (2) the frequent use of PIMs in patients with delirium. Thus, there is a need for improved understanding among healthcare providers about appropriate management of delirium in an acute care setting, which may benefit patients.

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