Association between comprehensive geriatric assessment and polypharmacy at discharge in patients with ischaemic stroke: A nationwide, retrospective, cohort study

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Summary

Background Polypharmacy and its adverse drug events are a major healthcare challenge related to falls, hospitalisations and mortality. Comprehensive geriatric assessment (CGA) may contribute to polypharmacy improvement, however, there is no clear evidence so far.

Methods Using a national inpatient database in Japan from April 1, 2014 to March 31, 2018, we investigated the association between CGA and polypharmacy. We identified patients aged ≥65 years admitted for ischaemic stroke who could receive oral medications. Propensity score matching was conducted for patients with and without CGA during hospitalisation. The outcomes were polypharmacy (defined as use of five or more types of oral medications) at discharge, the number of medication types prescribed at discharge, and the difference between the numbers of medication types prescribed on admission and at discharge.

Findings A total of 162,443 patients were analysed, of whom 39,356 (24·2%) received CGA, and propensity score matching identified 39,349 pairs. Compared with non-CGA group, the CGA group had a significantly lower proportion of polypharmacy at discharge (34·3% vs. 32·9%, $p < 0·001$) and a smaller number of medication types prescribed at discharge (3·84 vs. 3·76, $p < 0·001$).

Interpretation This study shows the clear evidence that there is a positive relationship between CGA and a reduction in the number of medications in older inpatients with ischaemic stroke.

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Keywords: Comprehensive geriatric assessment; Polypharmacy; Japanese diagnosis procedure combination database; Stroke; Older people

Introduction

Polypharmacy is a condition where a patient takes multiple medications or more medications than necessary. The most common definition of polypharmacy is use of five or more medications daily, although some studies define hyper-polypharmacy as use of 10 or more

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Research in context

Evidence before this study

We searched PubMed, Cochrane Library, and Japan Medical Abstracts Society databases with the terms "Comprehensive geriatric assessment" and "polypharmacy", up to Nov 30, 2021. Previous studies have shown the favourable effects of Comprehensive geriatric assessment (CGA) on healthcare and that its concept of identifying geriatric conditions might contribute to reductions in inappropriate prescribing, whereas there was no large-scale study to show it so far.

Added value of this study

This study answers the important question of whether CGA is associated with a reduction in the number of medications. Using a national inpatient database, with a robust design and strong statistical analyses, our findings suggested the effect of CGA on checking inappropriate prescription and reducing the number of medication types prescribed at discharge. From the results of subgroup analyses, we also indicated that this favourable effect might be pronounced in patients with polypharmacy. To our knowledge, this is the first evidence for the effect of CGA on prescription changes during hospitalisation.

Implications of all the available evidence

Correction of polypharmacy remains a major challenge in healthcare, given its negative clinical consequences. The present results suggest an additional role of CGA to prevent or improve polypharmacy. Development of healthcare systems that promote CGA implementation is warranted. This finding will contribute for health policy around the world.

medications.[1,2] In the USA, 36% of community-dwelling older persons had polypharmacy in 2010–2011, and this proportion was on the increase.[3] In Japan, about 40% of people aged ≥75 years were reported to have polypharmacy.[4] Ageing increases the risk of adverse drug events,[1] and the risks of drug–drug interactions increase with increasing number of medications.[5] Therefore, physicians need to consider the overall condition of patients when adding new medications, especially when the patients are older persons.[6] Correction of polypharmacy remains a major challenge in healthcare, given that polypharmacy increases healthcare costs.[7]

Several screening tools are commonly used to identify inappropriate prescriptions and reduce polypharmacy, including the Beers criteria, Screening Tool of Older People's Prescriptions criteria, and Screening Tool to Alert to Right Treatment criteria.[8–11] The Japan Geriatrics Society refined these criteria for Japanese people and published the "Guidelines for medical treatment and its safety in the elderly 2015".[12] The guidelines recommend that physicians minimise the number of medications, simplify drug regimens, limit the number of medication changes, and explain the reasons for prescribing medications well.

Comprehensive geriatric assessment (CGA) is widely defined as a multidimensional, multidisciplinary method to identify medical, social, and functional conditions of each older patient, and to develop an integrated/co-ordinated care plan.[13] Previous studies showed that CGA had favourable effects and that its concept of identifying geriatric conditions contributed to reductions in inappropriate prescribing.[14,15] Several studies suggested an effect of CGA on reducing polypharmacy.[16,17] However, the results were limited to outpatient settings and were not sufficiently adjusted for patient or hospital characteristics because of the small sample sizes.[16–18]

Stroke is a common disease among older persons that often causes disability or death. Early screening for rehabilitation and intervention is important in patients with stroke, and CGA may contribute to such screening.[19] Furthermore, various therapeutic medications are required for patients with ischaemic stroke to prevent recurrence after discharge, potentially leading to polypharmacy. In this study, we hypothesised the positive relationship between CGA and a reduction in the number of medications in older inpatients with ischaemic stroke and conducted a retrospective cohort study, using a national inpatient database in Japan.

Methods

Study design and participants

The Diagnosis Procedure Combination database is a national inpatient database for acute-care hospitals in Japan, the details of which were described previously.[15,20] The database includes administrative claims data and discharge abstract data collected from more than 1000 participating hospitals, and includes the following information: hospital identifier; patient age and sex; day of hospitalisation; emergency hospitalisation; main diagnosis, comorbidities at admission, and complications after admission encoded with International Classification of Diseases, 10th Revision (ICD-10) codes; surgical procedures; medications and devices used; prescriptions at discharge; length of hospital stay; and discharge status. The following data related to stroke are also available: Japan Coma Scale (JCS), modified Rankin Scale (mRS), date of stroke onset, Barthel Index (BI), oral intake and tube feeding status, and presence of dementia.[15]

The Reporting System for Functions of Medical Institutions is a hospital survey conducted annually by the Ministry of Health, Labour and Welfare of Japan. The survey includes the following hospital characteristics: location, type of hospital, number of beds,

emergency medical service system, and support system for discharge adjustment or home care. For the present study, we merged the 2014 survey data with data from the Diagnosis Procedure Combination database.

We used inpatient data from April 1, 2014 to March 31, 2018 and identified patients aged ≥65 years who were admitted for ischaemic stroke (ICD-10 code: I63) for the first time during the study period. We included patients with oral intake within 7 days of admission who were discharged alive to home. CGA is expected to be performed within 7 days of admission. Therefore, we excluded patients who were discharged within 7 days of admission. We also excluded patients whose data could not be merged with the Reporting System for Functions of Medical Institutions and patients with missing data on BI, mRS, date of stroke onset, or number of medications at discharge.

Study approval was obtained from the Institutional Review Board of the Graduate School of Medicine, The University of Tokyo. The need for informed consent was waived because of the anonymous nature of the data.

Variables

Patient baseline characteristics included age, sex, fiscal year of hospitalisation, emergency admission, JCS score, mRS score, date of stroke onset (≤3 days, 4−7 days, ≥8 days, asymptomatic), comorbidities, BI score, and presence of dementia. Data within 7 days of admission related to stroke care, namely medications (antiplatelets, anticoagulants, edaravone, hyperosmolar solutions, thrombolytics), endovascular procedures (thrombectomy, thrombolysis, percutaneous angioplasty, percutaneous stent placement) or surgical thrombectomy, and admission to special care units (intensive care unit, high care unit, stroke care unit) were also collected.[15]

JCS scores were categorised into four groups: 0 (alertness), 1−3 (dizziness), 10−30 (somnolence), and 100−300 (coma).[21] Comorbidities were converted to Charlson comorbidity index values based on Quan's algorithm, and categorised into five groups: 0, 1, 2, 3, and ≥4.[22] BI scores were categorised into six groups: ≤20 (bedridden), 21−40 (totally assisted/almost unable to perform tasks), 41−60 (partially assisted/tasks attempted but unsafe), 61−84 (moderate help required), 85−99 (minimal help required), and 100 (fully independent).

Hospitals were categorised into three groups based on number of general beds (small hospital: 20−99; medium hospital: 100−499; large hospital: ≥500) and type of hospital (university hospital, government-certified advanced hospital, other hospital). Existence of a discharge planning department, whether the hospital was a home care support hospital, and whether the hospital was a home care back-up hospital were also identified.

We extracted data for 88 types of frequently-prescribed medications or medications likely to cause adverse drug events in older persons.[10,12,23] A list of the medication types is presented in Supplementary Table 1. We followed the literature and categorised oral medications prescribed on the day of admission as follows[16,23−25]: antipsychotic drugs and hypnotics; antiarrhythmic drugs; hypotensive drugs and diuretics; gastrointestinal drugs; diabetes therapeutic drugs; analgesics; hyperlipemia medicines; anticoagulants and antiplatelets; Japanese herbal medicines; antidementia drugs; enteral nutrition; and other drugs considered inappropriate for older patients (e.g., anticholinergics, H1 receptor antagonists, antiemetics). Oral medications prescribed at discharge were identified and classified in the same manner.

Exposure and control

We divided the patients into a CGA group and a non-CGA group based on the claims data for CGA during hospitalisation. In the main analysis, all patients with ischaemic stroke were divided into a CGA group and a non-CGA group. In the first-step subgroup analysis, patients with ischaemic stroke with polypharmacy on admission were divided into a CGA group and a non-CGA group. In the second-step subgroup analysis, patients with ischaemic stroke with hyper-polypharmacy on admission were divided into a CGA group and a non-CGA group.

Outcomes

We defined polypharmacy as use of 5 or more types of oral medications from the 88 types of medications and hyper-polypharmacy as use of 10 or more types of oral medications. The primary outcome in the main analysis and first-step subgroup analysis was polypharmacy at discharge, while that in the second-step analysis was hyper-polypharmacy at discharge. The secondary outcomes in all analyses were: (i) number of medication types prescribed at discharge and (ii) difference between numbers of medication types prescribed on admission and at discharge.

Statistical analysis

First, we investigated the background characteristics of the patients without polypharmacy, patients receiving 5−9 medications, and patients receiving ≥10 medications on admission. We then compared the background characteristics between the CGA and non-CGA groups.

We conducted one-to-one propensity score (PS) matching between the CGA and non-CGA groups in the main, first-step subgroup, and second-step subgroup analyses.[15,26] For PS estimation, we used a logistic regression model with CGA as the function for patient background characteristics, hospital factors, and

total number and types of oral medications taken on admission. We additionally tried generalised estimating equation (GEE) approach with clustering by hospital for PS estimation.[27] We conducted a Hosmer–Lemeshow test to confirm the model calibration and calculated the C-statistic to evaluate the discriminatory ability of the model. Using the PS estimates, we conducted nearest-neighbour matching without replacement. The calliper was set at 0·2 times the standard deviation of the PS estimates. The variance ratios of the PS estimates were evaluated by an F-test, and standardised differences were used to compare characteristics between the two groups before and after matching. Standardised differences of >10% were regarded as imbalanced.[28] Outcomes were compared between the PS-matched patients in the CGA and non-CGA groups. Categorical variables are presented as numbers and percentages, and continuous variables are presented as means and standard deviations or medians and interquartile ranges. The Pearson chi-squared test was used for categorical variables, and the Wilcoxon signed-rank test was used for continuous variables. Risk differences and their 95% confidence intervals (CIs) were also calculated. All tests were two-sided, and statistical significance was defined as $p < 0·05$. All analyses were performed using Stata/SE version 17·0 (StataCorp, College Station, TX, USA).

Role of the funding source

The funders had no role in the execution of the study or the interpretation of the results. All authors had full access to all the data (including statistical reports and tables) in the study and SO had final responsibility for the decision to submit for publication.

Results

We identified 255,139 patients aged ≥65 years who were hospitalised for ischaemic stroke, had oral intake within 7 days of admission, and were discharged to home after ≥7 days of hospitalisation. The proportion of patients receiving CGA increased over time: 20·1% (10,189/50,571) before 2015, 22·3% (14,007/62,690) in 2015, 23·7% (15,856/67,000) in 2016, 25·8% (16,678/64,549) in 2017, and 28·7% (2960/10,329) in 2018. Of the 255,139 patients, 32,145 and 60,551 were excluded because of unavailable data for hospital characteristics and patient background characteristics, respectively. Consequently, a total of 162,443 patients with complete data were analysed, of whom 39,356 (24·2%) received CGA (Figure 1). The characteristics of the excluded patients are presented together with those of the analysed patients in Supplementary Table 2. The proportion of patients who received CGA was higher in the analysed patients.

The baseline characteristics of the patients receiving 5–9 drugs ($n = 30,318$; 18·7%) and ≥10 drugs ($n = 1687$; 1·0%) on admission were compared with those of patients without polypharmacy (Table 1). Patients aged 75–84 years, male patients, and patients with multimorbidity were likely to receive multiple medications.

The coefficients in the model for PS estimation are presented in Supplementary Table 3. The GEE model for PS estimation did not converge; therefore, we retained the original analysis to balance these important patient- and hospital-level variables. PS matching selected 39,349 pairs of CGA and non-CGA patients from the total patients with ischaemic stroke (main analysis). The Hosmer–Lemeshow test showed fair model calibration ($p = 0·051$), and the C-statistic for the logistic regression model was 0·632. There was no significant difference in the variance of the PS estimates between the two groups after matching (Supplementary Table 4). Table 2 shows the baseline characteristics of the patients in the CGA and non-CGA groups before and after PS matching in the main analysis. Before matching, the CGA group had more patients admitted on an emergency basis compared with the non-CGA group. The CGA group also had more comorbidities and were prescribed more medications compared with the non-CGA group. The proportions of patients admitted to large hospitals, non-university hospitals, and hospitals with support system for discharge planning or home care were higher in the CGA group compared with the non-CGA group. After PS matching, the distributions of the patient and hospital characteristics were well-balanced between the two groups. On average, the patients were prescribed 2–3 types of medications on admission. The types of oral medications on admission are also presented in Table 2. The three most frequently used medications were anticoagulants and antiplatelets, gastrointestinal drugs, and hypotensive drugs and diuretics. In the subgroup analyses, PS matching selected 8490 pairs from patients with polypharmacy (first-step subgroup analysis) and 455 pairs from patients with hyper-polypharmacy (second-step subgroup analysis). The C-statistics for the logistic regression models were 0·637 and 0·691 for the first-step and second-step subgroup analyses, respectively. The baseline characteristics were well-balanced after PS matching in both analyses (Supplementary Tables 5 and 6).

The outcomes of the PS-matched patients are shown in Table 3. In the main analysis, the proportion of patients with polypharmacy at discharge was significantly lower in the CGA group compared with the non-CGA group (32·9% vs. 34·3%; risk difference, −1·4% [95% CI −2·0% to −0·7%]; number needed to treat, 74 [95% CI 50 to 145]). In both groups, the number of medication types increased during hospitalisation. However, the increase was mildly, but significantly, lower in the CGA group compared with the non-CGA group (0·911 vs. 0·974, $p < 0·001$) and the mean number of

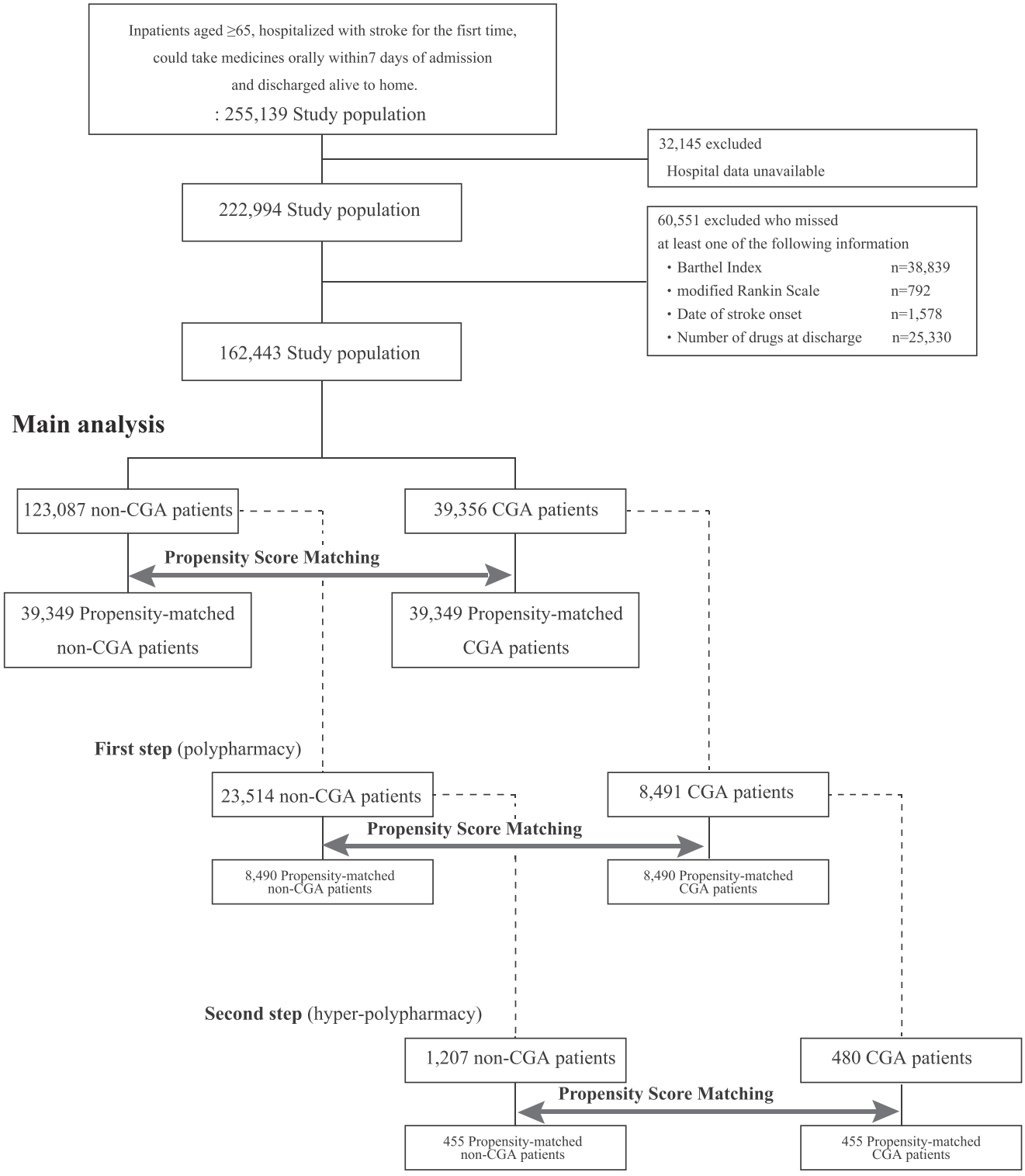

Figure 1. Flow diagram for the patient selection.
CGA: comprehensive geriatric assessment.

Characteristic	No polypharmacy, *n* (%)		5−9 medications, *n* (%)		≥10 medications, *n* (%)	
All	130,438		30,318		1687	
Age (years)						
65−74	50,274	(39)	11,110	(37)	620	(37)
75−84	52,210	(40)	13,062	(43)	762	(45)
85−94	25,737	(20)	5821	(19)	296	(18)
≥95	2217	(2)	325	(1)	9	(1)
Gender						
Male	76,039	(61)	18,277	(63)	1105	(63)
Female	54,399	(39)	12,041	(37)	582	(37)
Fiscal year of hospitalisation						
2014	38,061	(29)	5959	(20)	309	(18)
2015	35,146	(27)	5675	(19)	241	(14)
2016	31,944	(25)	8461	(28)	492	(29)
2017	25,287	(19)	10,223	(34)	645	(38)
Emergency admission	79,152	(61)	18,344	(63)	959	(64)
Japan Coma Scale						
Alertness	79,299	(61)	19,066	(63)	1071	(64)
Dizziness	45,679	(35)	10,402	(34)	570	(34)
Somnolence	4614	(4)	756	(3)	42	(3)
Coma	846	(1)	94	(0)	4	(0)
Modified Rankin Scale						
0	66,025	(51)	14,567	(48)	657	(39)
1	23,523	(18)	5859	(19)	390	(23)
2	15,558	(12)	4175	(14)	282	(17)
3	10,502	(8)	2703	(9)	177	(11)
4	10,633	(8)	2351	(8)	144	(9)
5	3041	(2)	426	(1)	29	(2)
Unknown	1156	(1)	237	(1)	8	(1)
Date of stroke onset						
≤3 days	112,246	(87)	25,550	(84)	1356	(80)
4−7 days	7087	(5)	1860	(6)	121	(7)
≥8 days	9416	(7)	2422	(8)	174	(10)
Asymptomatic	1689	(1)	486	(2)	36	(2)
Charlson comorbidity index						
0	85,949	(66)	18,148	(60)	866	(51)
1	8739	(7)	3112	(10)	246	(15)
2	28,013	(22)	6758	(22)	405	(24)
3	2901	(2)	1088	(4)	94	(6)
≥4	4836	(4)	1212	(4)	76	(5)
Barthel Index						
≤20	33,829	(26)	6889	(23)	364	(22)
21−40	13,367	(10)	3446	(11)	203	(12)
41−60	23,878	(18)	5807	(19)	346	(21)
61−84	14,964	(12)	3669	(12)	196	(12)
85−99	9,819	(8)	2336	(8)	137	(8)
100	34,581	(27)	8171	(27)	441	(26)
Dementia	34,674	(27)	8222	(27)	512	(30)
Comprehensive geriatric assessment	30,865	(24)	8011	(26)	480	(29)

***Table 1*: Baseline characteristics of the patients with and without polypharmacy on admission.**

Characteristic	CGA group before matching (*N* = 39,356)[†]		Non-CGA group before matching (*N* = 123,087)[†]		Standardised difference	CGA group after matching (*N* = 39,349)[†]		Non-CGA group after matching (*N* = 39,349)[†]		Standardised difference
Age (years)										
65–74	14,492	(37)	47,512	(39)	−3·7	14,491	(37)	14,453	(37)	0·2
75–84	16,169	(41)	49,865	(41)	1·2	16,166	(41)	16,020	(41)	0·8
85–94	8016	(20)	23,838	(19)	2·5	8013	(20)	8185	(21)	−1·1
≥95	679	(2)	1872	(2)	1·6	679	(2)	691	(2)	−0·2
Gender										
Male	22,790	(58)	72,631	(59)	−2·2	22,789	(58)	22,726	(58)	0·3
Female	16,566	(42)	50,456	(41)	2·2	16,560	(42)	16,623	(42)	−0·3
Fiscal year of hospitalisation										
2014	9106	(23)	35,223	(29)	−12·5	9106	(23)	8911	(23)	1·2
2015	9786	(25)	31,276	(25)	−1·3	9786	(25)	10,000	(25)	−1·3
2016	10,375	(26)	30,522	(25)	3·6	10,373	(26)	10,343	(26)	0·2
2017	10,089	(26)	26,066	(21)	10·5	10,084	(26)	10,095	(26)	−0·1
Emergency admission	25,885	(66)	72,570	(59)	14·1	25,880	(66)	25,739	(65)	0·8
Japan Coma Scale										
Alertness	23,594	(60)	75,842	(62)	−3·4	23,591	(60)	23,648	(60)	−0·3
Dizziness	14,106	(36)	42,545	(35)	2·7	14,103	(36)	14,053	(36)	0·3
Somnolence	1439	(4)	3973	(3)	2·4	1438	(4)	1434	(4)	0·1
Coma	217	(1)	727	(1)	−0·5	217	(1)	214	(1)	0·1
Modified Rankin scale										
0	18,685	(48)	62,564	(51)	−6·7	18,684	(48)	18,676	(48)	0·0
1	7861	(20)	21,911	(18)	5·6	7860	(20)	7694	(20)	1·1
2	5062	(13)	14,953	(12)	2·2	5061	(13)	5160	(13)	−0·7
3	3329	(9)	10,053	(8)	1·1	3327	(9)	3388	(9)	−0·6
4	3243	(8)	9885	(8)	0·8	3242	(8)	3221	(8)	0·2
5	876	(2)	2620	(2)	0·7	875	(2)	908	(2)	−0·6
Unknown	300	(1)	1101	(1)	−1·5	300	(1)	302	(1)	−0·1
Date of stroke onset										
≤3 days	34,200	(87)	104,952	(85)	4·7	34,195	(87)	34,263	(87)	−0·5
4–7 days	2383	(6)	6685	(5)	2·7	2381	(6)	2369	(6)	0·1
≥8 days	2283	(6)	9729	(8)	−8·3	2283	(6)	2242	(6)	0·4
Asymptomatic	490	(1)	1721	(1)	−1·3	490	(1)	475	(1)	0·3
Charlson comorbidity index										
0	24,551	(62)	80,412	(65)	−6·1	24,550	(62)	24,561	(62)	−0·1
1	3002	(8)	9095	(7)	0·9	3001	(8)	3067	(8)	−0·6
2	9150	(23)	26,026	(21)	5·1	9149	(23)	9104	(23)	0·3
3	1116	(3)	2967	(2)	2·7	1115	(3)	1071	(3)	0·7
≥4	1537	(4)	4587	(4)	0·9	1534	(4)	1546	(4)	−0·2
Barthel index										
≤20	9603	(24)	31,479	(26)	−2·7	9602	(24)	9520	(24)	0·5
21–40	3970	(10)	13,046	(11)	−1·7	3969	(10)	3898	(10)	0·6
41–60	7070	(18)	22,961	(19)	−1·8	7069	(18)	7047	(18)	0·1
61–84	4578	(12)	14,251	(11)	0·2	4578	(12)	4676	(12)	−0·8
85–99	3057	(8)	9235	(8)	1·0	3055	(8)	3136	(8)	−0·8
100	11,078	(28)	32,115	(26)	4·6	11,076	(28)	11,072	(28)	0·0
Dementia	10,898	(28)	32,510	(26)	2·9	10,896	(28)	10,954	(28)	−0·3
Number of medications taken on admission, mean (standard deviation)	2·8	(2·4)	2·6	(2·3)	3·9	2·8	(2·4)	2·9	(2·4)	−0·3
Oral medications on admission										
Anticoagulants and antiplatelets	27,356	(70)	81,052	(66)	7·8	27,349	(70)	27,341	(70)	0·0
Gastrointestinal drugs	18,874	(48)	55,777	(45)	5·3	18,869	(48)	18,901	(48)	−0·2

Table 2 *(Continued)*

Characteristic	CGA group before matching (*N* = 39,356)†		Non-CGA group before matching (*N* = 123,087)†		Standardised difference	CGA group after matching (*N* = 39,349)†		Non-CGA group after matching (*N* = 39,349)†		Standardised difference
Hypotensive drugs and diuretics	11,434	(29)	31,821	(26)	7·2	11,429	(29)	11,549	(29)	−0·7
Hyperlipemia medicines	10,106	(26)	29,773	(24)	3·4	10,105	(26)	10,100	(26)	0·0
Antipsychotic drugs and hypnotics	7286	(19)	20,254	(17)	5·4	7281	(19)	7376	(19)	−0·6
Analgesics	3859	(10)	10,457	(9)	4·5	3856	(10)	3790	(10)	0·0
Diabetes therapeutic drugs	3525	(9)	10,225	(8)	2·3	3524	(9)	3577	(9)	−0·5
Other drugs	2850	(7)	7829	(6)	3·5	2848	(7)	2896	(7)	−0·5
Japanese herbal medicines	1239	(3)	3569	(3)	1·5	1237	(3)	1253	(3)	−0·2
Antiarrhythmic drugs	1184	(3)	3453	(3)	1·2	1183	(3)	1183	(3)	0·0
Antidementia drugs	961	(2)	2,448	(2)	3·1	961	(2)	956	(2)	0·1
Enteral nutrition	24	(0)	85	(0)	−0·3	24	(0)	21	(0)	0·3
Use of drugs related to stroke care during hospitalisation										
Antiplatelets	30,661	(78)	91,705	(75)	8·0	30,654	(78)	30,719	(78)	−0·4
Anticoagulants	25,873	(66)	83,395	(68)	−4·3	25,870	(66)	25,883	(66)	−0·1
Edaravone	24,019	(61)	74,015	(60)	1·8	24,016	(61)	24,086	(61)	−0·4
Hyperosmolar solutions	2214	(6)	5489	(5)	5·3	2212	(6)	2199	(6)	0·1
Thrombolytics	1473	(4)	6137	(5)	−6·1	1473	(4)	1433	(4)	0·5
Endovascular procedures or surgical thrombectomy	470	(1)	1745	(1)	−2·0	470	(1)	493	(1)	−0·5
Hospitalised unit										
High care unit	1163	(3)	5125	(4)	−6·5	1163	(3)	1133	(3)	0·4
Stroke care unit	4993	(13)	15,038	(12)	1·4	4993	(13)	5093	(13)	−0·8
Intensive care unit	834	(2)	2882	(2)	−1·5	834	(2)	807	(2)	0·5
Hospital category (number of general beds)										
Small hospital (20–99)	2100	(5)	6547	(5)	0·1	2095	(5)	2094	(5)	0·4
Medium hospital (100–499)	24,059	(61)	80,171	(65)	−8·3	24,059	(61)	24,894	(61)	−0·8
Large hospital (≥500)	13,197	(34)	36,369	(30)	8·6	13,195	(34)	13,361	(34)	0·5
Type of hospital										
University hospital	1523	(4)	8159	(7)	−12·4	1523	(4)	1461	(4)	0·8
Government−certified advanced hospital	5394	(14)	14,003	(11)	7·0	5392	(14)	5410	(14)	−0·1
Other hospital	32,439	(82)	100,925	(82)	1·1	32,434	(82)	32,478	(83)	−0·3
Department for discharge planning	39,135	(99)	118,830	(97)	20·8	39,128	(99)	39,091	(99)	1·0
Home care support hospital	2155	(6)	3791	(3)	11·9	2150	(6)	2090	(5)	0·7
Home care back−up hospital	6425	(16)	12,016	(10)	19·6	6424	(16)	6360	(16)	0·4

***Table 2*: Baseline characteristics of the patients in the CGA and non-CGA groups before and after propensity score matching in the main analysis.**

† Data are shown as *n* (%) unless otherwise specified.

CGA, comprehensive geriatric assessment.

medication types prescribed at discharge was also significantly lower in the CGA group (3·76 vs. 3·84, $p < 0·001$).

In the first-step subgroup analysis for patients with polypharmacy on admission, the proportion of patients with polypharmacy at discharge was significantly lower in the CGA group compared with the non-CGA group (65·5% vs. 68·1%; risk difference, −2·6% [95% CI, −4·0% to −1·1%]; number needed to treat, 39 [95% CI, 25 to 88]). In these patients, the number of medications decreased during hospitalisation, and the reduction was more pronounced in the CGA group (−1·16 vs. −1·04, $p = 0·002$). The second-step subgroup analysis for patients with hyper-polypharmacy on admission showed no evidence of the differences in the proportion of patients with hyper-polypharmacy at discharge (CGA, 36·5% vs. non-CGA, 39·8%; risk difference, −3·3% [95% CI, −9·6% to 3·0%]; $p = 0·31$) or the reduction in number of medications (CGA, −3·2; non-CGA, −2·0; $p = 0·45$).

Discussion

Using a national inpatient database, the present study examined the association between CGA and polypharmacy at discharge among inpatients with ischaemic

Group	Outcome	Non-CGA group	CGA group	Risk difference	
				(95% CI)	*p*-value
All patients (39,349 pairs)	Polypharmacy at discharge, *n* (%)	13,491 (34·3)	12,959 (32·9)	−1·4 (−2·0 to −0·7)	<0·001
	Number of medication types prescribed at discharge, mean (SD)	3·84 (2·26)	3·76 (2·24)	−0·08 (−0·11 to 0·05)	<0·001
	Difference between numbers of medication types prescribed on admission and at discharge, mean (SD)	0·974 (2·55)	0·911 (2·53)	−0·06 (−0·10 to −0·03)	<0·001
Patients under polypharmacy on admission (8490 pairs)	Polypharmacy at discharge, *n* (%)	5779 (68·1%)	5562 (65·5%)	−2·6 (−4·0 to −1·1)	<0·001
	Number of medication types prescribed at discharge, mean (SD)	5·39	5·29	−0·10 (−0·17 to −0·02)	0·01
	Difference between numbers of medication types prescribed on admission and at discharge, mean (SD)	−1·04 (2·38)	−1·16 (2·40)	−0·11 (−0·18 to −0·04)	0·002
Patients under hyper-polypharmacy on admission (455 pairs)	Hyper-polypharmacy at discharge, *n* (%)	181 (39·8%)	166 (36·5%)	−3·3 (−9·6 to 3·0)	0·31
	Number of medication types prescribed at discharge, mean (SD)	7·71 (3·74)	7·60 (3·64)	−0·11 (−0·59 to 0·37)	0·65
	Difference between numbers of medication types prescribed on admission and at discharge, mean (SD)	−3·0 (3·65)	−3·2 (3·61)	−0·18 (−0·65 to 0·29)	0·45

***Table 3*: Outcomes in the CGA and non-CGA groups after propensity score matching.**
CGA, comprehensive geriatric assessment; CI, confidence interval; SD, standard deviation.

stroke. The GEE approach for PS estimation did not converge, which might be due to the relatively large number of patient- and hospital-level variables, considering the number of cases per hospital. PS-matching by the original analyses showed that CGA was associated with a decreased proportion of patients with polypharmacy at discharge. To our knowledge, this is the first evidence to show the positive relationship between CGA and polypharmacy correction during hospitalisation.

We have revealed the current status of prescriptions and polypharmacy among patients with ischaemic stroke in Japanese acute-care hospitals. The proportion of patients with polypharmacy was approximately 20% in our study cohort. This proportion was expectedly lower than the proportions in previous reports,[9,29] because the present study examined medications that are frequently prescribed and potentially inappropriate. We also confirmed that, reflecting the characteristics of patients with ischaemic stroke, lifestyle disease-related drugs, gastrointestinal drugs, antipsychotic drugs, and hypnotics were frequently prescribed.

CGA was conducted in 24·2% of patients in the study cohort. Although this proportion was low for a country with one of the most ageing populations worldwide, the proportion of patients receiving CGA gradually increased over time (22·3% in 2015 to 28·7% in 2018). Challenges related to CGA, such as staff shortages and the time-consuming nature, remain. More incentives for performance of CGA, increased frequency of workshops on CGA, or development of a simplified version of CGA may be important to increase CGA implementation.[30]

Notably, CGA was significantly associated with a lower proportion of patients with polypharmacy at discharge and a smaller number of medications prescribed at discharge. The percentage differences in polypharmacy at discharge between the CGA and non-CGA groups were 1·4% in all patients with ischaemic stroke and 2·6% in patients with polypharmacy on admission. CGA was reported to prevent frailty, reduce need for hospital care days, decrease mortality, and improve care for older persons.[31] The present results suggest an additional effect for preventing or improving polypharmacy.

Although statistically significant, the risk difference for polypharmacy and the difference in numbers of medication types between the CGA and non-CGA groups were relatively small in this study. It was reported that the components of CGA consistently include scales to evaluate cognitive function, activities of daily living, depression, vitality, social and economic situations, physical function, and nutritional aspects,[13,32] but it does not include specific screening tools related to prescriptions. Another explanation may be that patients after stroke required various oral medications to prevent recurrence and there was little room for drug reduction. To amplify the favourable effects on polypharmacy, further studies are needed to identify the components of CGA that contribute to polypharmacy

improvement or the group of patients who experience more benefits.[32] Integration of convenient screening tools for prescriptions into CGA may also be important.

Prescription adjustments conducted in geriatric evaluation and management units were shown to correct inappropriate prescriptions and reduce polypharmacy.[33] However, these special units are not always available, and the problem of polypharmacy also needs to be addressed in general wards. CGA is performed in general wards in Japan, and we used an inpatient database that covers hospitals nationwide. Our findings using real-world data suggest that CGA can also play an important role in general wards.

Some limitations must be considered when interpreting the results of this study. First, we did not extract all prescription details but focused on frequently prescribed medications and potentially inappropriate medications. We did not have data on other drugs, supplements, or over-the-counter drugs. Moreover, the data on medications were extracted as medication types and did not necessarily equal the number of medications. We extracted 88 types of medications, covering most of the inpatient prescriptions (>80%),[23] and were able to distinguish different types of medicines belonging to the same category (e.g., sulfonylurea and biguanide within diabetes therapeutic drugs). However, two or more drugs within the same type were not distinguishable (e.g., two or more sulfonylureas). Nevertheless, we assume that such cases were rare. Second, this was an observational study using an administrative database. Although high specificity for the diagnosis of cerebrovascular diseases was reported for the database,[34] there was no validation study for the diagnosis of stroke in particular. In addition, the data lacked information on the detailed clinical conditions (e.g., severity of disease, experience of adverse drug reactions, frailty), the social or economic background characteristics of the patients and whether the patients had received CGA in the past. Moreover, some patients were excluded because of missing data, and it was not possible to tell whether these data were missing at random. Whereas there may be some bias caused by the exclusion, age, sex, or the proportion of polypharmacy on admission were similar and we assumed that the impact of missing numbers was minimal. Although we used PS matching to adjust for numerous measured confounders, PS matching only accounts for observed covariates and there remains a possibility of residual confounding.

In this study using a large national inpatient database in Japan, CGA in inpatients with ischaemic stroke was associated with a decreased proportion of patients with polypharmacy at discharge. Thus, development of healthcare systems that promote CGA implementation is warranted. Further studies are expected to clarify the components of CGA that are associated with polypharmacy improvement or the group of patients who derive the most benefit from CGA.

Contributors

TH, HYamana, HT, HYasunaga, and SO designed the study. KF and HYasunaga acquired the data. TH, HYamana, HT, HYasunaga, and SO were responsible for the underlying data verification and performed the analyses. All authors contributed to the interpretation of the data. TH drafted the manuscript and the other authors revised it for important intellectual content. All authors approved the final draft of the manuscript for submission. All authors had full access to all the data (including statistical reports and tables) in the study and SO had final responsibility for the decision to submit for publication.

Data sharing statement

The dataset analysed in the current study is not publicly available because of contracts with the hospitals providing data to the database.

Declaration of interests

All authors declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; and no other relationships or activities that could appear to have influenced the submitted work.

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Supplementary materials

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