*Original Article*

# Potentially inappropriate medications at admission among elderly patients transported to a tertiary emergency medical institution in Japan

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*Aim:* Potentially inappropriate medications (PIMs) have been reported to be associated with lower adherence, higher rates of adverse events, and higher health-care costs in elderly patients with high comorbidity. However, inappropriate prescribing has not been adequately reported in studies of patients transported to tertiary care hospitals. In this study, we investigated PIMs at the time of admission, on the basis of the prescription status of elderly patients admitted to a tertiary emergency room (ER).

*Methods:* We included 316 patients (168 men and 148 women, aged 75–97 years) who were admitted to our ER from September 2018 to August 2019, whose prescriptions were available on admission. Drugs that met the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP) criteria version 2 were defined as PIMs. The primary outcome was the proportion of older adults taking at least one PIM at admission.

*Results:* The proportion of patients taking PIMs at admission was 57% (n = 179). The most common PIMs were benzodiazepines, proton pump inhibitors, and nonsteroidal anti-inflammatory drugs. The total number of medications prescribed at admission, prescriptions from multiple institutions, and prescriptions from clinics were the risk factors for PIMs at admission ($P < 0.01$, $P < 0.001$, and $P < 0.001$, respectively).

*Conclusion:* We must be careful to avoid inappropriate prescribing for patients transported to tertiary care hospitals who have numerous prescriptions at the time of admission, patients who receive prescriptions from multiple medical institutions, and patients who receive prescriptions from clinics.

**Key words:** Critical care, emergency room, potentially inappropriate medication, screening tool of older persons' potentially inappropriate prescriptions, tertiary hospital

## BACKGROUND

POTENTIALLY INAPPROPRIATE MEDICATIONS (PIMs) are known as medications with a higher risk of adverse effects than expected. They should be avoided by the elderly, especially when safer alternative prescriptions are available in similar circumstances.[1] Potentially inappropriate medications are associated with adverse drug events, hospitalization, mortality, and increased health-care costs.[2–6] Correction of PIMs is important in the elderly, who are more susceptible to adverse drug events.

Screening tools for detecting PIMs and patient backgrounds vary, and it has been reported that the rate of PIMs use in elderly patients at admission or visit to the emergency room (ER) is approximately 29%–45%.[7–9] Regarding studies comparing Beers criteria with the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP) criteria, some studies have reported that the STOPP criteria had a higher detection rate of PIMs,[10,11] whereas others reported that the Beers criteria had a higher detection rate of PIMs.[12] However, the STOPP criteria have

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been reported to be more strongly associated with adverse drug events than the Beers criteria,[10] which can screen PIMs in 3 min, suggesting its usefulness.[11] Moreover, many drugs were listed in the STOPP criteria in the Japanese market, and the STOPP criteria in Japan were deemed to have a great merit. However, studies on PIMs applying the STOPP criteria in Japan have focused on patients receiving home care.[13,14] Recently, the number of elderly patients who are transported to ER for intensive care has been increasing.[15–17] However, in Japan, PIMs at the time of admission (using STOPP criteria) have not been studied in the elderly who are transported and admitted to tertiary care hospitals. Therefore, this study aimed to investigate the prescription status of elderly patients admitted to Japan's tertiary ERs using the STOPP criteria, as well as the frequency, features, and factors associated with PIMs on admission.

## METHODS

### Ethics statement

APPROVAL FOR THIS study was obtained from the research ethics committee of Tokyo Medical University (Approval No. T2020-0377), and this study was carried out in accordance with the Declaration of Helsinki. Data obtained only from medical records were used. There was no contact with the patients; hence, the requirement of informed consent was waived.

### Study design and setting

This retrospective observational study was undertaken at Tokyo Medical University Hospital (a 904-bed tertiary institution) between August 2018 and September 2019. Patients were admitted to the emergency intensive care unit (EICU) or a general ward of the hospital. Patients in the EICU receive intensive care.

### Participants

This study included elderly patients aged 75 years or more who were admitted to our tertiary care emergency medical institution. Patients who passed away in the ER, those transferred to another hospital directly from our ER, those hospitalized at our department for less than 24 h, and those with unknown medications were excluded.

### Data collection

The data about age, sex, primary diagnosis at admission, social and medical history, and medication use were collected from the electronic medical records of Tokyo Medical University Hospital. Information regarding medication use at the time of admission at our hospital was according to prescriptions and referral letters provided by the attending physician at the outpatient department of the referring medical institution. Prescriptions on admission included all regular oral, inhalant, and injectable medications used at discharge. Potentially inappropriate medications were identified using the STOPP criteria version 2.[18]

### Outcomes

The primary outcome was the proportion of patients taking at least one PIM at admission. Moreover, we assessed PIMs on admission by drug type, and the investigated factors associated with PIMs on admission.

### Statistical analysis

A nonparametric test was used to examine associations between the use of PIMs at admission and selected variables. By referring to other studies carried out previously,[1,18,19] the variables included in the nonparametric test were age, sex, total number of medications at admission, prescriptions from multiple health-care providers, prescriptions from clinics, Acute Physiology and Chronic Health Evaluation (APACHE) II score, and Charlson comorbidity index (CCI). Analyses were carried out using SPSS software version 24 (IBM). A *P*-value of less than 0.05 was considered statistically significant.

## RESULTS

### Patient selection and patient characteristics

DURING THE STUDY period, 704 patients who were 75 years and older were transferred to the ER of our hospital. Altogether, 388 patients were excluded from the study for the following reasons: less than 24 h of hospital stay (from ER to hospitalization) ($n$ = 230), death at the outpatient department ($n$ = 132), and absence of medication data ($n$ = 26). Thus, only 316 patients were included in the final analysis (Fig. 1).

Table 1 shows the baseline characteristics of the patients. The mean age of the patients was 84 years (standard deviation [SD], 5.8); 53% ($n$ = 168) were men. The mean CCI was 2.1 (SD, 1.9) and the mean APACHE II score was 19 (SD, 4.7). The primary diagnoses were exogenous ($n$ = 38 [12%]) and endogenous ($n$ = 278 [88%]). The most common endogenous disease was heart failure ($n$ = 48 [15%]). Thirty-eight patients with exogenous diseases consisted of

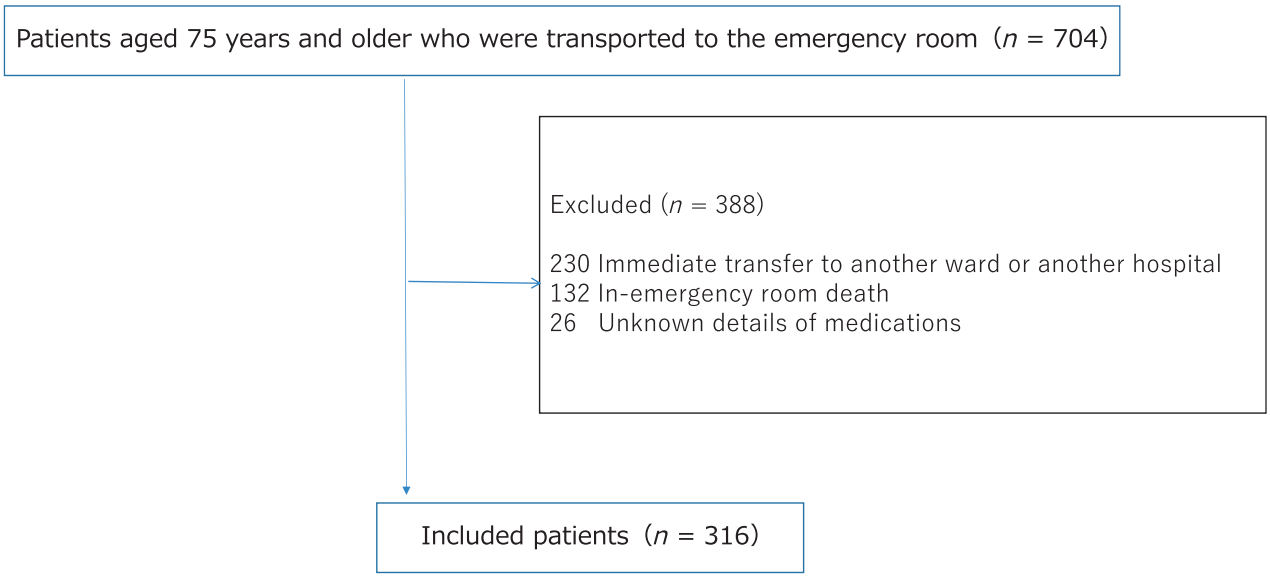


**Fig. 1.** Flowchart of patient inclusion in this study of potentially inappropriate medications among elderly individuals transported to a tertiary emergency medical institution in Japan.

**Table 1.** Participants' baseline demographic and clinical characteristics

| Variable | (*n* = 316) |
|---|---|
| Age at enrolment, years | 84 ± 5.8 |
| Men | 168 (53) |
| Charlson comorbidity index at enrolment | 2.1 ± 1.9 |
| APACHE II score | 19 ± 4.7 |
| Admission diagnosis | |
| Endogenous disease | 278 (88) |
| Heart failure | 48 (15) |
| Ischemic stroke | 36 (11) |
| Pneumonia | 33 (10) |
| Septic shock | 22 (7) |
| Post-cardiac arrest syndrome | 20 (6) |
| ACS | 14 (4) |
| Sepsis | 11 (3) |
| Exogenous disease | 38 (12) |
| Admitted wards | |
| Emergency intensive care unit | 267 (84) |
| General wards | 49 (16) |

*Note*: Data are reported as mean ± standard deviation or *n* (%).
Abbreviations: ACS, acute coronary syndrome; APACHE II, Acute Physiology and Chronic Health Evaluation II.

30 with trauma, 2 with burns, 2 with hypothermia, 2 with asphyxia, 1 with heatstroke, and 1 with acute drug intoxication. In addition, 84% (*n* = 267) of the patients were admitted to the EICU and 16% (*n* = 49) were admitted to the general wards.

## Potentially inappropriate medications by primary disease type

Table 2 shows the number and percentage of patients with PIMs, including each primary disease. Potentially inappropriate medications were included in 61% (*n* = 170) of patients with endogenous diseases and 23% (*n* = 9) with exogenous diseases. Potentially inappropriate medications were included in 46% (*n* = 22) of patients with heart failure, 25% (*n* = 9) with stroke, 30% (*n* = 10) with pneumonia, 45% (*n* = 10) with septic shock, 25% (*n* = 5) with post-cardiac arrest syndrome, and 21% (*n* = 3) with acute coronary syndrome.

## Potentially inappropriate medications prescribed at admission and predictors of PIMs at admission

Table 3 shows the patients' PIMs at admission, by drug subcategory. The total number of PIMs on admission was 273. The most common PIMs on admission were benzodiazepines, proton pump inhibitors, and nonsteroidal anti-inflammatory drugs. These three categories were considered to account for 40% of the total PIMs used at admission and

**Table 2.** Proportion of elderly patients taking potentially inappropriate medications (PIMs) at admission according to their primary diagnosis for admission

| Primary diagnosis for admission | Proportion of patients taking PIMs, *n* (%) |
|---|---|
| Total, *n* = 316 | |
| Endogenous disease, *n* = 278 | 170 (61) |
| Heart failure, *n* = 48 | 22 (46) |
| Ischemic stroke, *n* = 36 | 9 (25) |
| Pneumonia, *n* = 33 | 10 (30) |
| Septic shock, *n* = 22 | 10 (45) |
| Post cardiac arrest syndrome, *n* = 20 | 5 (25) |
| ACS, *n* = 14 | 3 (21) |
| Exogenous disease, *n* = 38 | 9 (23) |

Abbreviation: ACS, acute coronary syndrome.

**Table 3.** Number of potentially inappropriate medications at admission by type of drug

| | At admission |
|---|---|
| Total | 273 |
| Benzodiazepines | 48 (18) |
| Proton pump inhibitors | 34 (12) |
| NSAIDs | 27 (10) |
| Laxatives | 25 (9) |
| Mucosal protective drugs | 19 (7) |
| Vitamin preparations | 16 (6) |
| Antiplatelets | 15 (5) |
| Antihistamines | 13 (5) |
| Antipsychotics | 13 (5) |
| Hypnotics (nonbenzodiazepines) | 11 (4) |

*Note*: Data are reported as *n* (%). Potentially inappropriate medications were defined based on the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions criteria version 2.
Abbreviation: NSAID, nonsteroidal anti-inflammatory drug.

discharge. Furthermore, 57% ($n$ = 179) of patients were taking at least one PIM at the time of transport to hospital.

Table 4 compares the following: (i) the difference between the presence of PIMs and the median number of prescriptions at admission (Mann–Whitney test: $P < 0.01$), (ii) the association of the prescriptions from multiple health-care providers and the presence of PIMs at admission ($\chi^2$-test: $P < 0.001$), and (iii) the association of the prescriptions from clinics and the presence of PIMs at admission ($\chi^2$-test: $P < 0.001$). The presence of PIMs at admission was associated with the total number of prescriptions at hospital admission, prescriptions from multiple health-care providers, and prescriptions from clinics.

## DISCUSSION

### Frequency of PIMs

THIS IS THE first study to use the STOPP criteria to investigate PIMs on admission in elderly patients transported to a tertiary emergency medical center in Japan. In this study, 57% of patients were taking at least one PIM at the time of admission. Compared with the Beers criteria, which reported that 29% of elderly patients visiting tertiary care hospitals in urban areas had PIMs,[7] the incidence of PIMs in this study was high. This could be because the STOPP criteria have a higher chance of detecting PIMs than the Beers criteria[10,11] and because the availability of the drugs listed in the STOPP criteria is greater than that listed in the Beers criteria, which might have affected the results. Moreover, the fact that this study included people aged 75 years and older, whereas people aged 65 years and older are often defined as elderly in other countries, could have affected the results. In Japan, this definition of the elderly is being reconsidered. The Japan Geriatrics Society, the Japan Gerontological Society, and the Japanese guidelines for medications define elderly as individuals aged 75 years and older.[20,21] Therefore, only patients aged 75 years and older were included in the analysis.

### Association between primary diseases and PIMs

Approximately half of the patients with heart failure and septic shock had PIMs on admission. The high prevalence of PIMs in patients with heart failure is consistent with that of previous reports.[22] The association between septic shock and PIMs on admission has not been reported previously because PIMs on admission might not have been previously validated in critically injured patients in tertiary emergency care facilities.

### Factors associated with PIMs on admission

In this study, PIMs taken by patients admitted to tertiary care hospitals were associated with the total number of

**Table 4.** Predictors of potentially inappropriate medications (PIMs) at admission

| Patient/institutional variables | All patients | PIMs group | Non-PIMs group | *P*-value |
|---|---|---|---|---|
| Age, median (IQR) | 84 (79–88) | 85 (79–88) | 84 (78–88) | 0.291 |
| Sex, female/male (*n*) | 148/168 | 85/94 | 63/74 | 0.307 |
| No. of medications at admission, median (IQR) | 6 (4–9) | 7 (5–10) | 4 (3–6) | <0.010 |
| Prescriptions from multiple health-care providers, *n* (%) | 48 (100) | 46 (96) | 2 (4) | <0.001 |
| Prescriptions from clinics, *n* (%) | 160 (100) | 117 (73) | 43 (27) | <0.001 |
| APACHE II score, median (IQR) | 18 (15–24) | 19 (15–25) | 18 (13–24) | 0.082 |
| Charlson comorbidity index, median (IQR) | 2 (1–3) | 2 (1–3) | 2 (1–3) | 0.563 |

*Note*: Data are reported as mean ± standard deviation or *n* (%). PIMs were defined based on the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions criteria version 2.
Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; IQR, interquartile range.

prescriptions on admission, prescriptions from multiple health-care providers, and prescriptions from clinics.

In primary care, it has been reported that the total number of prescriptions correlates with the presence of PIMs.[23] But the same result was observed in elderly patients who were transported to tertiary care hospitals. It has also been reported that PIMs are associated with receiving prescriptions from multiple physicians in primary care.[23] In this study, PIMs were associated with prescriptions from multiple medical institutions. The use of a medication handbook and coordination with a family dispensing pharmacy are ways to avoid PIMs when prescribing from multiple medical institutions. However, some patients have multiple medication handbooks and family dispensing pharmacies. It was therefore difficult for physicians and pharmacists to keep track of all the drugs prescribed by other physicians; it is believed that they were unable to review the drugs and adjust the prescriptions as needed.

Furthermore, the inclusion of clinics in the medical institutions attended by patients correlated with PIMs at the time of admission. Hospitalization is an opportunity to review and optimize the management of chronic diseases in the elderly. It has been reported that admission to a geriatric unit can reduce PIMs.[24] However, in clinics without inpatient facilities, it is difficult for a physician to coordinate all prescriptions within a limited amount of time. Prescriptions in clinics are often reported to be a continuation of drugs prescribed by other medical institutions.[25] Additionally, an association has been reported between the presence of PIMs and a lack of specialized medical care.[26] These reasons could be responsible for the association between the presence of PIMs and prescriptions from clinics.

The association between multimorbidity and polypharmacy as well as between the CCI and health-care costs has been reported,[27,28] and we speculated that PIMs are more common in patients with more severe illnesses and comorbidities. However, no association was observed between APACHE II or CCI and PIMs on admission because patients who do not regularly attend medical institutions and do not receive prescriptions could become seriously ill and be transported to the tertiary care institutions.

In recent years, the issue of adverse drug events due to polypharmacy has been addressed by governments and media. Yet, according to our results, PIMs are still an issue, not only in primary care but also in tertiary emergency medical institutions. Medical institutions responsible for the care of critically ill elderly patients need to be aware of the presence of PIMs in the drug schedule of admitted patients who take a large number of drugs, visit a large number of medical institutions, or receive prescriptions from clinics. Solving the problem of inappropriate prescribing requires sharing knowledge among all health-care professionals, including emergency physicians and intensivists, not just physicians in the prescribing clinic. Furthermore, rather than tackling the problem through a specific hospital doctor or a specific department, multiple departments, family medical institutions, and medium-to-large hospitals must collaborate in the review of individual patients.

## Limitations

Our results should be interpreted with awareness of some limitations. First, this study used a retrospective design that could have biased the data. Our results should be confirmed in other hospitals. Second, the study did not investigate inappropriate underprescribing, which could put patients at risk. Third, this study was limited to patients transported to a single facility; the results cannot be generalized. These findings should be investigated in other hospitals. Fourth, this study focused on elderly patients aged 75 years and older;

however, in other countries, elderly patients are often defined as those aged 65 years and older. Therefore, the results of this study cannot be simply compared with those of other global studies. Finally, in this study, we used the STOPP criteria version 2. However, drugs lack clinical importance and prevalence even within the STOPP criteria.[18] Moreover, it has been reported that the evidence on the clinical and economic impact of the STOPP/START criteria is limited.[19]

## CONCLUSIONS

WE MUST BE cautious about inappropriate prescribing for elderly patients who are transported and admitted to a tertiary care hospital. This includes patients with a large number of prescriptions at admission, patients who receive prescriptions from multiple medical institutions, and patients who are prescribed from clinics.

## DISCLOSURE

APPROVAL OF THE research protocol: Approval for this study was obtained from the medical ethics committee of our institution (No. T2020-0377), and this study was conducted in accordance with the Ethical Guidelines for Epidemiological Research in Japan.

Informed consent: Individual informed consent requirement was waived because this was a retrospective analysis of data collected prospectively for routine care. There was no breach of privacy or anonymity.

Registry and registration no. of the study/trial: The datasets used and analyzed in the current study are available from the corresponding Scientific Editor on reasonable request.

Animal studies: N/A.

Conflict of interest: None.

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