Original Article

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Low rate of pharmacists accessing renal function laboratory values: A cross-sectional study using electronic medical records of a Japanese community pharmacy

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SUMMARY: This study aimed to assess the availability of renal function laboratory values in Japanese community pharmacies and examine their association with the prescription of drugs requiring dosage adjustment. In this cross-sectional observational study, data were obtained from the electronic medical records of a community pharmacy in Japan. A total of 389 eligible patients (aged ≥ 18 years) who visited the pharmacy in April 2024 were included. The primary outcome measures were the proportion of participants with available renal function laboratory values and those prescribed medications requiring dosage adjustment. A total of 128 patients (32.9%) were prescribed at least one medication requiring dosage adjustment, most commonly vitamin A and D preparations (32 cases) and antidiabetic agents (31 cases). Renal function laboratory values were available for 40 patients (10.3%). Compared to those not prescribed such drugs, patients receiving medications requiring renal-based dosage adjustments included a significantly higher proportion of older adults (70/128, 54.7% *vs* 98/261, 37.5%, $p = 0.001$) and patients with available laboratory values (20/128, 15.6% *vs* 20/261, 7.7%, $p = 0.015$). No patients were identified with the "Triple Whammy," which is known to significantly increase the risk of renal function deterioration. Community pharmacists endeavor to obtain renal function laboratory values for older adults, who are more likely to be prescribed medications requiring dosage adjustment. However, the proportion of cases with obtained laboratory values remains low. Pharmacists are expected to actively recommend renal function testing to physicians. Furthermore, they should contribute to safe pharmacotherapy by utilizing comprehensive patient information.

Keywords: community pharmacy services, renal insufficiency, patient safety, aged

1. Introduction

The kidneys play a pivotal role in maintaining fluid homeostasis and excreting waste products. Chronic kidney disease (CKD) is defined as a condition characterized by structural or functional abnormalities of the kidney—such as glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2 or albuminuria ≥ 30 mg per 24 hours—persisting for more than three months (*1*). The global prevalence of CKD is estimated at approximately 13.4% and continues to rise (*2,3*). In Japan, approximately 20% of adults (about 19.9 million people) are estimated to have stages 3–5 CKD (*4*). Patients with CKD represent a population with significant opportunities for therapeutic intervention, as they frequently have comorbidities such as diabetes, hypertension, and dyslipidemia. Moreover, because most patients with CKD have mild to moderate disease (stages 1–3), they can typically be managed by general practitioners in outpatient rather than inpatient settings (*2*). As of October 1, 2023, there were 36.23 million people aged 65 years or older in Japan, accounting for 29.1% of the total population. Renal function declines with age, highlighting the importance of considering age-related changes in healthy older individuals (*5*). With Japan's rapidly aging population, the number of patients with impaired renal function is expected to increase. In addition to estimated GFR (eGFR), estimated creatinine clearance (eCCr) based on serum creatinine (Cr) is commonly used to assess renal function in clinical practice. The eCCr, calculated using the Cockcroft-Gault formula based on serum Cr levels, age, gender, and weight, is commonly used to determine drug dosage. Community pharmacies are in a key position to prevent adverse events, as they frequently fill prescriptions for patients with impaired

renal function. However, community pharmacies often lack access to laboratory values related to patients' renal function (*6*). In Japan, a system utilizing the "My Number Card" has allowed healthcare professionals, including community pharmacists, to access annual health checkup results since October 2021. However, updates are often delayed, and available data typically date back about a year.

A decline in renal function leads to elevated blood concentrations of renally excreted drugs, thereby increasing the likelihood of adverse drug reactions (*7*). Many drugs require dosage adjustment in patients with impaired renal function (*8*). Community pharmacists are not sufficiently involved in dosage adjustment based on renal function (*9*). Nevertheless, appropriate dosage adjustment is essential to prevent adverse events caused by overdose in patients with renal impairment. Therefore, in Japan, community pharmacies commonly refer to the 37th edition of the Dosage Recommendations for Drugs That Require the Most Attention in Renal Impairment, published by the Japanese Society of Nephrology and Pharmacotherapy (JSNP) (*10*). This list is freely accessible and widely used in hospitals and pharmacies, as it is distributed at no cost in accordance with the intentions of the academic society.

A major cause of drug-induced kidney injury is the use of glycopeptide antibiotics or non-steroidal anti-inflammatory drugs (NSAIDs) (*11*). Specifically, a rapid decline in renal function occurring within a few hours to days is commonly referred to as acute kidney injury (AKI). Approximately a decade ago, a study reported that the concurrent use of three specific drug classes—renin-angiotensin system (RAS) inhibitors, which include angiotensin-converting enzyme inhibitors (ACE-Is) and/or angiotensin receptor blockers (ARBs), diuretics, and NSAIDs—increases the risk of AKI, a phenomenon known as the 'Triple Whammy' (*12*). Since these drugs are all commonly prescribed, monitoring this combination is crucial. Community pharmacists, who can manage medications prescribed by multiple clinics, play an essential role in this process by applying their expertise.

When community pharmacies adjust dosages based on renal function, laboratory values are essential for appropriate decision making. Community pharmacists must identify drugs requiring dosage adjustment and determine which patients have been prescribed them. However, prescription patterns requiring renal-based dosage adjustments and the availability of relevant laboratory values remain unclear in clinical practice. This study aims to quantify drugs requiring renal-based dosage adjustment and identify the number of patients prescribed them at the Keio University Community Pharmacy. This single-center, retrospective cross-sectional study was conducted not to provide a national estimate, but to describe the profile of high-risk drugs, the sources of laboratory data, and prescription combination patterns in a real-world community pharmacy. The findings of this study will enhance pharmacists' awareness of renal dose adjustment and support the provision of appropriate drug therapy.

2. Materials and Methods

2.1. Study design

We conducted a cross-sectional study to investigate how renal function laboratory values are utilized in pharmacies, referencing a large volume of patient medication records from a single community pharmacy. Patient age, sex, availability of renal function laboratory values, their sources, and prescribed medications were extracted and entered into an Excel spreadsheet for analysis. Renal function laboratory values in this study were assessed using eGFR, Cr, and blood urea nitrogen (BUN). A list of drugs requiring renal-based dosage adjustment was created to analyze the prescribed medications. From the pharmacy's drug list, medications included in the 'Dosage Recommendations for Drugs That Require the Most Attention in Renal Impairment, 37th Edition' were selected. This reference, published by the JSNP, was compiled using data from prescription drug package inserts.

2.2. Study population

Information about the study was disclosed within the pharmacy, and patients were given the opportunity to decline participation through an opt-out procedure. Medication histories of patients who visited the Keio University Community Pharmacy with prescriptions between April 1 and April 25, 2024, were included. Patients under 18 years were excluded due to the use of a different renal function estimation formula in this age group. Homebound patients were not included in the study population because there was no direct interaction with them at the pharmacy. Furthermore, patients receiving only topical prescriptions were not included in the study population, because these medications do not require renal-based dosage adjustment.

2.3. Statistical analysis

Drug classification was performed using the system published by the Ministry of Health, Labour and Welfare (MHLW), and the number of drugs per therapeutic category was visualized through simple tabulation. Renal function data were considered available if at least one of eGFR, BUN, or Cr was obtainable. For the analysis of age-related differences, patients were categorized into "older adults" (aged ≥ 65 years) and "non-older adults" (aged 18–64 years). The availability of renal function data and the proportion of older adults were analyzed using Pearson's chi-squared test in Microsoft Excel.

The normality of eGFR values was assessed using the Shapiro–Wilk test, and the equality of variances was assessed using the F-test in RStudio. Based on these assessments, eGFR values were compared between older and non-older adults using a two-sided Student's *t*-test. Box plots were generated using RStudio software (version 2026.01.1+403; Posit Software, PBC, Boston, MA, USA). A p-value < 0.05 was considered statistically significant. The number of patients prescribed each drug class involved in the Triple Whammy was illustrated using a Venn diagram.

2.4. Ethics approval

The study protocol was submitted to and approved by the Ethics Committee of the Faculty of Pharmacy, Keio University (approval No. 241113-1). Information about the study was disclosed within the pharmacy, and individuals were given the opportunity to decline participation through an opt-out procedure.

3. Results

3.1. Adopted medications requiring renal dose adjustment in the pharmacy

This study aimed to calculate the proportion of renal function laboratory values recorded in medication histories at a community pharmacy. Prior to initiating the study, a list of pharmacy-adopted medications requiring dose adjustments based on renal function was created using a drug list published by the JSNP (Figure 1). The medications were categorized according to their therapeutic classification. The Keio University Community Pharmacy adopted 1,521 pharmaceutical products, including different dosage forms of the same active ingredients. From these, only oral medications and liquid preparations were extracted, resulting in 1,239 products. When grouped by ingredients, the total decreased to 697, of which 57 ingredients (8.2%) matched those on the JSNP list. The Keio University Community Pharmacy carried 148 products containing the 57 identified ingredients, accounting for 12% of the 1,239 listed products.

The drugs were categorized into 23 therapeutic classes (Figure 2). Among them, the most common were 26 antidiabetic agents, 19 central nervous system agents, 16 vitamin A and D preparations, and 10 anticoagulants. Diabetic nephropathy develops because of vascular damage caused by hyperglycemia in diabetes mellitus. Therefore, patients with these conditions require closer monitoring.

3.2. Characteristics of patients included in this study

Patients who visited the Keio University Community

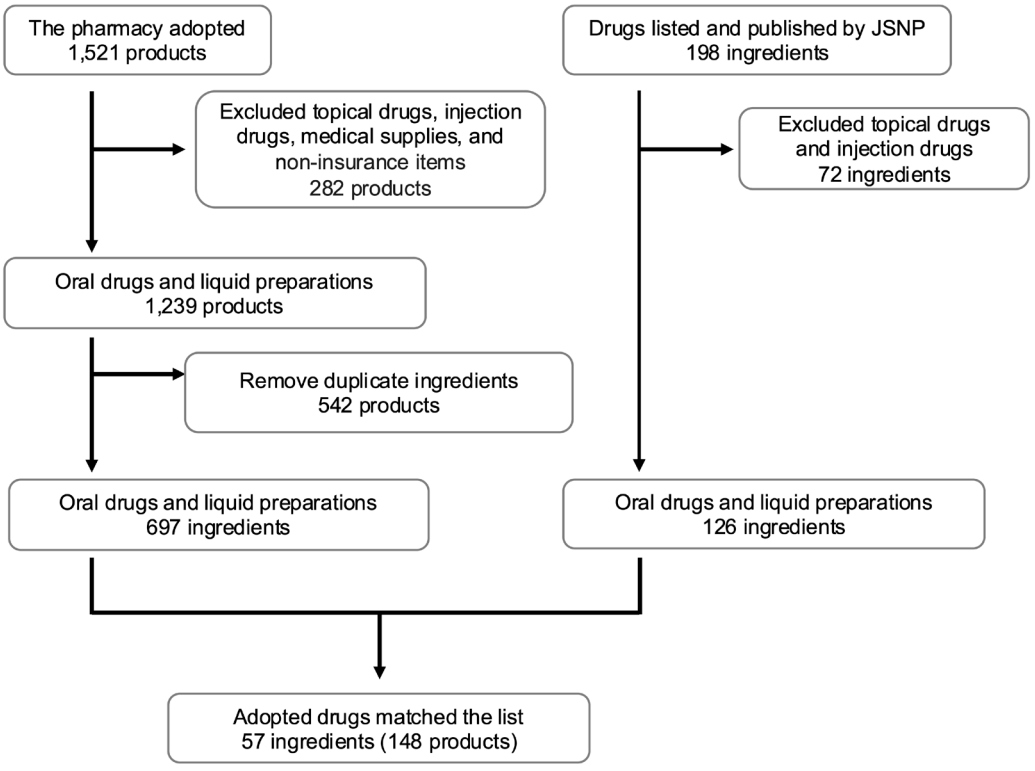

Figure 1. Scheme of the process of comparing pharmacy-adopted drugs with the renal function adjustment drug list. A scheme depicting the process of comparing drugs adopted by the pharmacy with the renal function adjustment drug list published by the JSNP. The number of products, including dosage variation, is noted for each ingredient and product name.

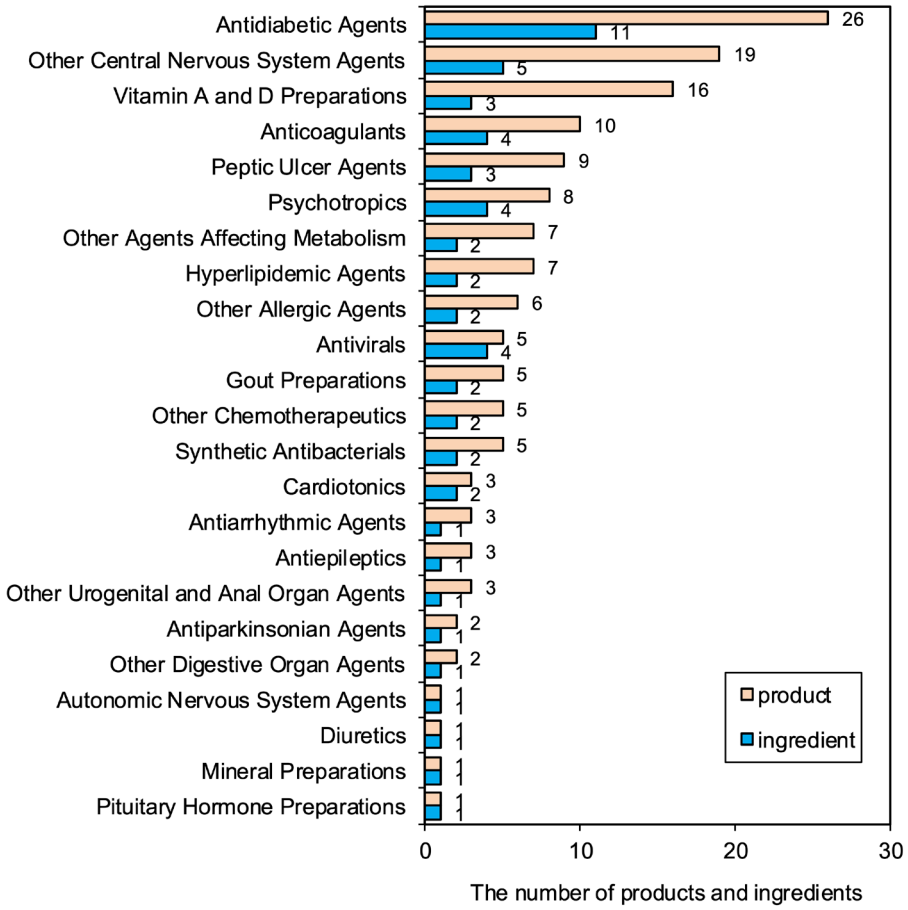

Figure 2. The number of products and ingredients requiring dose adjustment is categorized by the therapeutic classification. The drug classification information system published by the MHLW was used to categorize the data. A bar graph summarizes the product names and the number of ingredients in descending order for each therapeutic category.

Pharmacy after April 1, 2024, were selected in order of their visits. Medication records were collected for a total of 403 patients who met the study population criteria. Fourteen patients under 18 were excluded, as the eGFR calculation differs between adults and minors. Consequently, 389 patients were included in this study. Table 1 shows the characteristics of these 389 patients. Among them, 193 (49.6%) were male, and 196 (50.4%) were female. When categorized by age group, 221 (56.8%) were non-older adults and 168 (43.2%) were older adults. Among older adults, 89 (22.9%) were early-stage, and 79 (20.3%) were late-stage. The average number of drugs per patient was 4.4 ± 2.8, and 114 patients (29.3%) met the criteria for polypharmacy, defined as taking six or more medications. Additionally, 128 patients (32.9%) were taking at least one of the listed drugs. Among these, 8 patients (2.1%) took the highest number of listed drugs, with three drugs each.

Table 1. Characteristics of patients included in this study (*n* = 389)

	n (%)
Gender	
Male	193 (49.6)
Female	196 (50.4)
Age	
18-64	221 (56.8)
≥ 65	168 (43.2)
Number of drugs	
1-5	275 (70.7)
6-9	92 (23.7)
≥ 10	22 (5.7)
Number of prescriptions for listed drugs	
0	261 (67.1)
1	98 (25.2)
2	22 (5.7)
3	8 (2.1)

3.3. The availability of renal function laboratory values and their sources

Table 2 presents the availability and sources of renal function laboratory values, including eGFR, BUN, and Cr. A total of 40 patients (10.3%) had at least one available laboratory value. Among these, 34 patients (8.7%) had eGFR values, which are essential for dose adjustment in pharmacies. Laboratory values came from three sources: blood test results sheets brought by patients, electronic health records accessed *via* the

Table 3. Total number of prescriptions for listed drugs

Pharmacological Classification	Ingredient
Vitamin A and D Preparations (32)	Eldecalcitol (24), Alfacalcidol (5), Vitamin A (3)
Antidiabetic Agents (31)	Metformin (10), Glimepiride (8), Sitagliptin (6), Anagliptin/Metformin (2), Vildagliptin/Metformin (2), Alogliptin (1), Imeglimin (1), Nateglinide (1), Alogliptin/Pioglitazone (0), Pioglitazone/Metformin (0), Trelagliptin (0)
Peptic Ulcer Agents (19)	Famotidine (12), Cimetidine (4), Sulpiride (3)
Gout Preparations (13)	Allopurinol (11), Colchicine (2)
Other Central Nervous System Agents (11)	Pregabalin (5), Mirogabalin (4), Acamprosate (0), Memantine (1), Tiapride (1)
Psychotropics (11)	Duloxetine (5), Mirtazapine (3), Venlafaxine (2), Risperidone (1)
Other Allergic Agents (10)	Levocetirizine (9), Fexofenadine/Pseudoephedrine (1)
Hyperlipidemia Agents (9)	Fenofibrate (7), Bezafibrate (2)
Anticoagulants (8)	Edoxaban (5), Apixaban (1), Dabigatran (1), Rivaroxaban (1)
Synthetic Antibacterials (7)	Sitafloxacin (4), Levofloxacin (3)
Other Agents Affecting Metabolism (4)	Methotrexate (2), Risedronic acid (2)
Other Urogenital and Anal Organ Agents (4)	Tadalafil (4)
Antivirals (3)	Valacyclovir (3), Entecavir (0), Famciclovir (0), Oseltamivir (0)
Antiarrhythmic Agents (2)	Atenolol (2)
Antiepileptics (1)	Levetiracetam (1)
Pituitary Hormone Preparations (1)	Desmopressin (1)
Antiparkinsonian Agents (0)	Amantadine (0)
Autonomic Nervous System Agents (0)	Distigmine (0)
Cardiotonics (0)	Digoxin (0), Metildigoxin (0)
Diuretics (0)	Acetazolamide (0)
Mineral Preparations (0)	Potassium Chloride (0)
Other Chemotherapeutics (0)	Fluconazole (0), Trimethoprim/Sulfamethoxazole (0)
Other Digestive Organ Agents (0)	Metoclopramide (0)

Table 2. Availability of renal function laboratory values and their sources

	n (%)
Not available	349 (89.7)
Available	40 (10.3)
Laboratory Report	30 (75.0)
Specific Health Checkup information	7 (17.5)
Prescription	3 (7.5)

My Number System, and prescriptions containing laboratory values. Community pharmacists scanned these documents and attached them to medication records. The most common source was blood test result sheets. Thirty patients (75.0%) provided laboratory values to the pharmacy through this method.

3.4. Prescription of listed drugs

Table 3 provides a summary of drugs requiring dosage adjustment according to renal function, categorized by therapeutic class and specific ingredients. The listed drugs were prescribed a total of 166 times. Drugs from 16 therapeutic categories were prescribed. Vitamins A and D were the most frequently prescribed category, administered to 32 patients. The most frequently prescribed drug was Eldecalcitol (24 times), followed by Famotidine (12 times) and Allopurinol (11 times). Among the listed drugs, antidiabetic agents represented the category with the highest number of entries (Figure 2). Antidiabetic agents were prescribed to 31 patients, making them the second most frequently prescribed therapeutic category.

3.5. Characteristics of patients who were prescribed the listed drugs

A total of 389 patients were divided into two groups: those prescribed listed drugs (prescribed group, 128 patients) and those not prescribed these drugs (non-prescribed group, 261 patients) (Table 1). Renal function laboratory values were available for 15.6% of patients in the prescribed group (20/128) and 7.7% in the non-prescribed group (20/261), with a significantly higher proportion in the prescribed group (χ^2 test, $p = 0.015$) (Figure 3A). However, despite the high risk of overdose in the prescribed group due to renal impairment, approximately 85% of these patients lacked renal function laboratory data. Additionally, the relationship between listed drug prescriptions and age is shown in Figure 3B. Among the 128 patients in the prescribed group, 54.7% (70 patients) were older adults, compared to 37.5% (98/261) in the non-prescribed group. The proportion of older adult patients was significantly higher in the prescribed group (χ^2 test, $p = 0.001$). Additionally, the medical institutions that issued laboratory values were categorized. Among the 33 patients, clinics were the most common source (18 patients). A similar pattern was observed for test sheets. Conversely, all prescriptions accompanied by laboratory values were issued by university hospitals (Figure 3C). Access to electronic health check-up records (7 patients) was excluded, as it was unrelated to the prescribing institution.

3.6. Association between eGFR and listed drug prescription in older adults

Among the various indicators of renal function, eGFR is the most important and can be directly used for dose adjustment in cases of renal impairment. In the prescribed group, 19 of 128 patients (14.8%) provided their eGFR to the pharmacy, compared to 15 of 261 patients (5.7%) in the non-prescribed group, showing a significant difference (χ^2 test, $p = 0.003$) (Figure 4A). The relationship between the availability of eGFR and age is shown in Figure 4B. Among the 34 patients who provided their eGFR, 21 (61.8%) were older adults. In contrast, among the 355 patients without their eGFR data, 147 (41.4%) were older adults, representing a significantly lower proportion than those who provided their eGFR (χ^2 test, $p = 0.022$). Figure 4C shows the actual eGFR values for 34 patients, divided into non-older adults (*13*) and older adults (*21*). The mean eGFR in non-older adults was 76.0 ± 16.0 mL/min/1.73m², compared to 64.1 ± 17.5 mL/min/1.73m² in older adults, but the difference was not statistically significant (two-sided *t*-test, $p = 0.063$). Prior to this analysis, it was confirmed that there was no significant deviation from normality or inequality of variances, ensuring the appropriateness of the parametric test. These findings indicate that older adults tend to have lower renal function than non-older adults and that renal function declines with age, necessitating caution in drug dosage. Furthermore, among the 34 patients with available eGFR, 9 (2 non-older adults and 7 older adults) had eGFR values below 60 mL/min/1.73m², meeting the diagnostic criteria for CKD. These nine patients represent a subgroup requiring particular caution in drug dosing (below the dotted lines).

3.7. Evaluation of acute kidney injury due to Single, Double, Triple Whammy

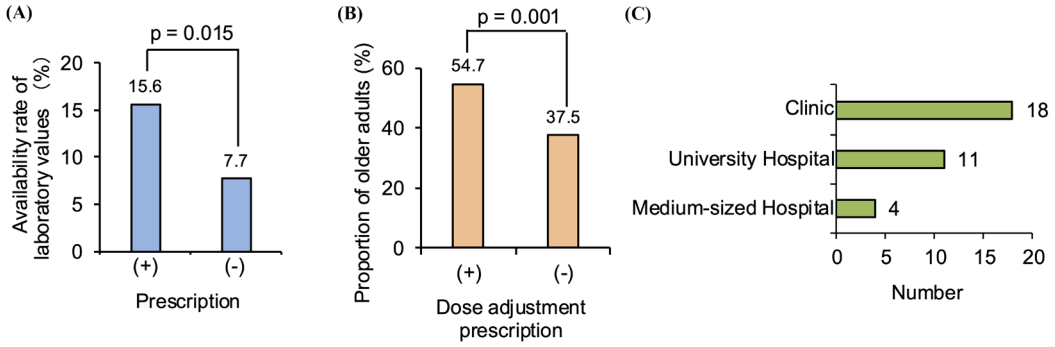

Figure 3. The relationship between the availability of renal function laboratory values, medications requiring dose adjustments, and age. (A) Comparison of the proportion of patients with available laboratory values between those prescribed at least one drug requiring dosage adjustment and those not prescribed such drugs. The p-values calculated using Pearson's chi-squared test are shown in the figure. **(B)** Comparison of the proportion of older adults between those prescribed at least one drug requiring dosage adjustment and those not prescribed such drugs. **(C)** The healthcare institutions that issued prescriptions with laboratory values and those that provided clinical laboratory values are categorized by their size and depicted in a bar graph. Seven individuals are not included in the figure due to their specific health check-up information being obtained through the company listed on their "My Number Card."

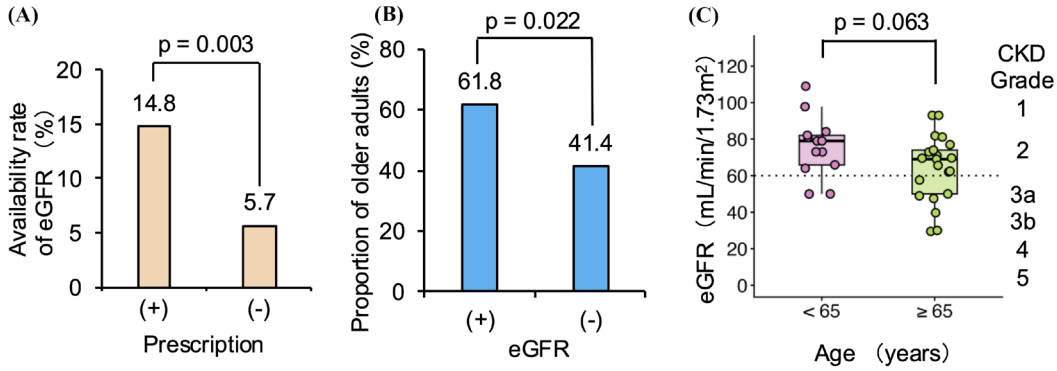

Figure 4. The relationship between the availability of eGFR, medications requiring dose adjustments, and age. (A) Comparison of the proportion of patients with eGFR values between those prescribed at least one drug requiring dosage adjustment and those not prescribed such drugs. The p-values calculated using Pearson's chi-squared test are shown in the figure. **(B)** The proportion of older adults in groups with and without available eGFR values is depicted in the bar graph. **(C)** The eGFR values between older adults and non-older adults were compared using a box plot. The dotted line indicates the threshold requiring dosage adjustment for most listed drugs (eGFR < 60 mL/min/1.73 m²). The CKD risk classification based on eGFR values ranged from Grade 1 to 5. The p-values calculated using the *t*-test are shown in the figure.

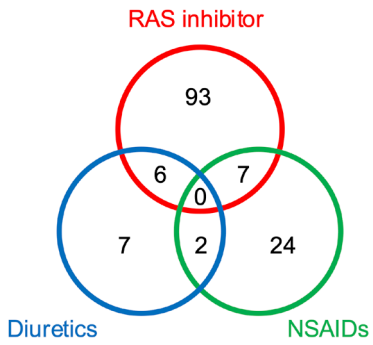

Figure 5. Number of patients with Single, Double, Triple Whammy Risk. The number of patients prescribed RAS inhibitors, diuretics, and NSAIDs is counted and presented using a Venn diagram. The numbers are based on the prescription of 389 patients, including those who were prescribed multiple drugs. A total of 250 patients who were not prescribed any of these drugs are excluded from the diagram.

Use of one, two, or all drug classes—RAS inhibitors, diuretics, and NSAIDs—was defined as Single, Double, and Triple Whammy, respectively. Notably, except for diuretics acetazolamide, RAS inhibitors, and NSAIDs were not included among the listed drugs. The number of patients classified as Single, Double, and Triple Whammy was 124 (31.9%), 15 (3.9%), and 0 (0%), respectively (Figure 5). The largest group consisted of 250 patients (64.3%) who did not fall into any of these categories. Among patients classified as Single or Double Whammy, ARBs were commonly used as RAS inhibitors—for example, azilsartan (28 patients) and telmisartan (27 patients). Among diuretics, furosemide—a loop diuretic—was the most frequently used and prescribed to seven patients. Loxoprofen sodium hydrate, the most commonly used NSAID in Japan, was prescribed to 18 patients. Among patients classified as Double Whammy, the most common drug combination was RAS inhibitors and NSAIDs (seven patients), followed by RAS inhibitors and diuretics (six patients), diuretics and NSAIDs (two patients). No patients were prescribed RAS inhibitors, diuretics, and NSAIDs concurrently by different medical institutions.

4. Discussion

Renal function laboratory values are unfamiliar and not widely recognized among the public. However, these values are critical for the safe use of medications, as their absence can lead to life-threatening consequences. In August 2011, Boehringer Ingelheim Japan issued a safety alert, commonly known in Japan as a 'Blue Letter' due to its distinctive blue paper, for the anticoagulant Pradaxa Capsule. The alert reported 139 cases of severe bleeding potentially related to the drug, including 15 fatalities. Among these, 49 cases involved renal impairment, and 22 patients had contraindicated clearance levels (eCCr < 30 mL/min). Access to Cr values in pharmacies might have enabled pharmacists to assess the drug's appropriateness. Previous studies have reported that 88.4% of community pharmacists find it difficult to obtain patients' laboratory values (*9*). Therefore, this study aimed to assess the availability and consideration of renal function laboratory values in Japanese community pharmacies. A list of drugs requiring dosage adjustment is publicly available from the JSNP and is widely used in both hospitals and community pharmacies in Japan. In this study, we examined the extent to which listed drugs are included in Keio University Community Pharmacy and identified the most common therapeutic categories. Excluding topical medications, 57 ingredients accounting for 148 of 1,239 adopted products (12%), were included in the list of drugs requiring renal function laboratory values for prescription auditing (Figure 1). These drugs fell into 16 categories, classified by therapeutic type (Figure 2). The community pharmacy in this study receives prescriptions from over 100 medical institutions monthly, covering a wide geographical area and diverse medical specialties. Therefore, the data in this study are considered generalizable. Among the listed drugs, antidiabetic agents were most prevalent, comprising 11 ingredients (26 products) (Figure 2). Additionally, antidiabetic agents such as metformin, glimepiride, and sitagliptin were prescribed 31 times among the 389 patients, accounting for approximately 8.0% (Table 3). This number of prescriptions ranked them the second most frequently prescribed category after vitamin A and D agents. A study using Japan's medical insurance data reported that approximately 20% of patients with diabetes experienced rapid renal function decline, 1.2 times higher than patients without diabetes (*13*). Furthermore, since diabetic nephropathy is the most common underlying condition in patients on dialysis, monitoring renal function in individuals with diabetes is essential (*14*). Based on the clinical prioritization perspective, antidiabetic agents should be prioritized for information sharing, as they are frequently prescribed and require careful management of renal function. In this study, eldecalcitol was the most frequently prescribed drug (Table 3). Furthermore, in the Japanese Adverse Drug Event Report (JADER) database, eldecalcitol was the second most frequently suspected drug for acute kidney disease, following valacyclovir hydrochloride (*15*). Therefore, it is crucial to monitor not only calcium levels but also renal function. Additionally, osteoporosis affects 15.9 million people in Japan, and its prevalence increases with age (*16*). In Japan's aging society, where community pharmacies play an essential role, this drug should continue to be carefully monitored.

Nearly half of pharmacists identified the lack of patients' renal function data as a barrier to dose adjustment (*6*). In this study, it was shown that the proportion of renal function laboratory values obtained from community pharmacies was 10.3% (40/389; Table 2). A nationwide survey in Japan reported a

renal function verification rate of 5.5% in community pharmacies, which was numerically close to that observed in the present study (*17*). This finding highlights the lack of renal function information, which poses a significant barrier to appropriate dose adjustment. Currently, structured systems for real-time data sharing between clinics and community pharmacies are not widely established in the Japanese healthcare system. Consequently, the most common and practical method for pharmacists to obtain laboratory data is for patients to voluntarily present paper-based reports from medical institutions. To overcome this barrier and facilitate proactive recommendations to physicians, utilizing digital infrastructure is essential. While specific health check-up data can currently be accessed *via* the national ID system (My Number Card), integrating clinical laboratory values into more accessible digital platforms, such as electronic medication notebooks or Personal Health Records, is required. This would allow pharmacists seamless access to patient data without placing an extra communication burden on physicians. Furthermore, the obtained eGFR values revealed that older patients had lower values than non-older patients (Figure 4C). It is well known that kidney function declines with age, and a similar tendency was observed in our study (*4*). These findings indicate that pharmacists should pay particular attention to reviewing laboratory values in older adults. The proportion of older adults was significantly higher in the group with available eGFR values compared to the group without (Figure 4B). This finding suggests that pharmacists may already be actively seeking laboratory values for older adults with expected renal decline. Moreover, as the number of regularly used drugs increases with age, older adult patients are more likely to have chronic diseases and undergo routine medical visits and blood tests, making it easier to obtain laboratory values (*18*). While many community pharmacists find it difficult to obtain patients' laboratory values, findings suggest that they attempt to acquire such values for patients requiring special caution (*4,6*). Currently, including laboratory values on prescriptions is not mandatory in Japan; rather, it is positioned as an advanced initiative by specific institutions, such as university hospitals, to enhance information sharing with pharmacies. Although patients often receive their test results in printed form, the majority do not fully understand the importance of having pharmacists review these values. Regarding patient characteristics, laboratory values are easier to obtain from a specific group of patients who proactively wish to review their results together with healthcare professionals. To shift from this limited access to comprehensive confirmation, the widespread adoption of electronic prescriptions and enhanced integration of laboratory values and diagnoses will be a potential solution. In the context of real-world practice, more immediate and realistic improvement strategies include hospitals and clinics attaching key laboratory values directly to prescriptions and pharmacies utilizing standardized interview templates during medication history taking to systematically screen the available test results. Strengthening local collaboration and internal workflow standardization will be vital until a fully integrated digital infrastructure is established. The concomitant use of RAS inhibitors, diuretics, and NSAIDs is referred to as the "Triple Whammy." This combination synergistically reduces renal blood flow and glomerular filtration pressure, ultimately leading to kidney injury. The National Institute of Health Sciences (NIHS) issued repeated Drug Safety Information warnings in 2003, 2006, and 2013 regarding the "Triple Whammy." They highlighted that this combination should be avoided due to its high risk of causing kidney injury, especially in older adults, individuals with existing renal impairment, and those with hydration issues. In particular, their 2013 warning spotted that the combination of three drugs poses a higher risk of causing acute kidney injury compared to the combination of two drugs. In this study, no patients met the criteria for Triple Whammy (Figure 5). Additionally, a previous study by Imai *et al*. reported that only 0.3% of patients met the criteria for Triple Whammy (*19*). However, a study using the JADER database reported that approximately half of the patients who developed AKI were taking the Triple Whammy drugs, and another report stated that the risk of AKI increases 1.3-fold due to Triple Whammy (*20,21*). Therefore, community pharmacies must remain vigilant. This study showed that all 15 patients who met the criteria for Double Whammy were prescribed two drugs by the same medical institution. For these patients, particular attention should be paid to the possibility of a third drug being prescribed by a different department. Furthermore, NSAIDs are widely used as over-the-counter (OTC) drugs in Japan. In this study, six patients were using RAS inhibitors and diuretics. Community pharmacists should consider not only prescriptions from medical institutions but also comprehensive patient information. Reports suggest that pharmacists' access to clinical laboratory data improves medication accuracy management, enabling community pharmacists to contribute to safe pharmacotherapy (*22*). A study involving 199 CKD patients reported that active vitamin D preparations were significantly more common in the adverse reaction group, leading some to suggest that this should be called the "Fourth Whammy (*23*)." In our study, eldecalcitol was the most commonly used preparation (Table 3). This finding indicates that further investigation is necessary, including monitoring the course of patients taking this drug.

5. Limitations

This study has several limitations. First, it is a retrospective study based on medication histories, which may omit prescribed drugs and laboratory

values. Additionally, although a drug is recorded in the medication history, it is unclear whether the patients actually took it. Second, some renal function laboratory values may not reflect the most current data. In particular, laboratory values from the Specific Health Check-up accessed *via* the My Number system require time to be updated. Therefore, the laboratory values used in this study may not accurately reflect patients' current renal function. Consequently, temporal changes in renal function must be considered when interpreting the study's results. Finally, only prescribed drugs data from medical histories were collected, so information on temporarily used OTC drugs may be missing.

6. Conclusion

This study suggested that community pharmacists should obtain renal function laboratory values for older adults, who are more likely to be prescribed medications requiring dose adjustment. However, only about 10% of cases had available laboratory values. Antidiabetic agents and vitamin A and D agents were commonly prescribed, underscoring the importance of verifying renal function in these cases. Although no patients met the criteria for Triple Whammy, 139 out of 389 patients (35.7%) were considered at risk. Furthermore, it is desirable that national guidelines for pharmacy-based point-of-care testing be expanded in the future to include renal function parameters. This would enable pharmacists to directly assess patient status and provide evidence-based recommendations. In the future, it will be necessary to proactively suggest the need for testing to physicians. Creating an environment that enables community pharmacists to access patients' laboratory values and proper medication management, including not only prescribed drugs but also OTC drugs, can be ensured, and community pharmacists can contribute to safe pharmacotherapy.

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