Nonsteroidal anti-inflammatory drugs use in patients with chronic kidney disease are often prescribed from different clinicians than those who diagnosed them

Running title: NSAIDs in patients with CKD

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Key points

1. In Japan, nonsteroidal anti-inflammatory drugs (NSAIDs) are often prescribed to patients with chronic kidney disease (CKD) by departments that are different from those that diagnosed CKD;

2. We used the Japanese health insurance claims database to analyze the frequency of difference in departments of diagnosis and prescription;

3. Among patients with CKD, 50.4% received CKD diagnosis and NSAID prescription from different departments;

4. CKD diagnoses were mostly from internal medicine departments, whereas NSAIDs were often prescribed by other departments and institutions;

5. NSAIDs are often prescribed to patients with CKD from different clinicians than those who diagnosed them.

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Abstract

Purpose: When prescribing nonsteroidal anti-inflammatory drugs (NSAIDs) for chronic kidney disease (CKD), patients' pathology and concomitant medications should be considered. In our pharmaceutical experience, NSAIDs are often prescribed by departments that are different from those that diagnosed CKD. That is, NSAIDs may be prescribed for patients without the advice of the clinicians who diagnosed them. In this study, we aimed to elucidate how frequently such cases occur.

Methods: We used the large health insurance claims database constructed by JMDC Inc., Tokyo. We evaluated the proportions of CKD diagnosis and NSAID prescription by different clinical departments and institutions.

Results: A total of 224 014 out-patients were included in the analysis; they were divided into CKD (n = 1501) and non-CKD groups (n = 222 513). The internal medicine departments diagnosed CKD most frequently (74.8% of the patients) and surgical departments rarely diagnosed CKD. However, the proportion of prescribed NSAIDs was high in other departments, especially surgical departments. In the CKD group, 50.4% of the patients received CKD diagnosis and NSAID prescription from different clinical departments; 72.8% of the patients received a diagnosis and prescription from different medical institutions.

Conclusion: Our study revealed that NSAIDs are often prescribed to patients with CKD from different clinicians than those who diagnosed them.

Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) are reportedly associated with acute kidney injury (AKI) in the general population and chronic kidney disease (CKD) progression [1-3]. The typical mechanism of kidney injury from NSAIDs involves reduced renal plasma flow caused by a decrease in prostaglandins [4]. Thus, the KDIGO 2012 Clinical Practice Guidelines for the Evaluation and Management of Chronic Kidney Disease (KDIGO guidelines) provide the following recommendations for the use of NSAIDs (including nonselective and selective cyclooxygenase (COX)-2 inhibitors) in patients with CKD [5]: (1) should be avoided in people with a glomerular filtration rate (GFR) of <30 ml min^{-1} 1.73 m^{-2}, (2) prolonged therapy is not recommended in people with a GFR of <60 ml min^{-1} 1.73 m^{-2}, (3) should not be used in people taking lithium, and (4) should be avoided in people taking renin-angiotensin-aldosterone system (RAAS) blockers. These recommendations are also included in the Japanese guidelines [6]. Thus, clinicians should prescribe NSAIDs with attention to CKD pathology and concomitant medications.

In our pharmaceutical practice experience, NSAIDs are often prescribed by different departments than those that diagnose the patient with CKD. For example, CKD may be diagnosed by an internal medicine department, whereas NSAIDs may be prescribed by

an orthopedic surgery department. That is, NSAIDs may be prescribed without the advice of the clinicians who diagnosed CKD. To the best of our knowledge, no study has assessed the frequency of this phenomenon.

The frequency and patterns of NSAID usage by patients with CKD have been examined by several researchers. Zhan *et al*. examined the usage of over-the-counter and prescription NSAIDs for 12 065 adults in the United States of America and found that 5.0% of the patients with moderate to severe CKD used NSAIDs daily for 30 d or more [7]. Hull *et al*. surveyed 12 011 patients with identified CKD (stages 3–5) in the United Kingdom and reported that 11.1% of the patients with CKD were prescribed NSAIDs in the same year and that the prescription proportions decreased gradually with the stage of CKD [8]. In addition, Heleniak *et al*. studied 12 065 adult patients in Poland and found that 16.9% of the patients used NSAIDs daily, or several times a week; the average number of tablets taken within a month was 21.8 [9]. These studies suggest that NSAIDs are being used inappropriately in patients with CKD. However, the real-world usage of NSAIDs by patients with CKD in Japan remains unclear. As Japan has an excellent public health insurance system, out-of-pocket medical fees paid by patients only reach 30% of the total medical cost [10]. Therefore, many Japanese visit medical institutions even with a common cold and do not use over-the-counter medication [11]. In other words, it is considered that

the prescription status of the insurance claims directly reflects the actual use of medicines in comparison to that in other countries. Therefore, elucidation of the prescription status of NSAIDs in patients with CKD in Japan is considered important.

In this study, we aimed to elucidate the current situation regarding differences in CKD diagnosis and NSAID prescription among clinical departments using the health insurance claims database in Japan. In addition, we evaluated patterns of NSAID usage by patients with CKD and compared this with use by patients without CKD.

Methods

Data sources

We used the health insurance claims database constructed by JMDC Inc., Tokyo [12]. This is a nationwide database of completely anonymized individual records. The JMDC database comprises monthly claims from medical institutions and pharmacies since January 2005. In June 2018, this database comprised approximately 5.6 million insured persons aged 0–74 years, with mainly company employees and their family members, representing approximately 5% of the population in Japan.

Study population and data collection

Adult out-patients (aged ≥20 years) who were newly prescribed orally administered NSAIDs from January 2016 to March 2016 (observation period) were selected. To detect new NSAID prescriptions, we screened data from 24 months before the study period, that is, January 2014 to December 2015 (screening period). In addition, patients who were diagnosed with CKD during the observation and screening periods were enrolled for the secondary analysis. To calculate the duration of regular use of NSAIDs, we followed prescription continuity from the start of NSAID use to March 2017. NSAIDs were identified using the Anatomical Therapeutic Chemical (ATC) system, code M01A1. Clinical departments and institutions that diagnosed CKD and prescribed NSAIDs were identified based on text codes and institution IDs. For a detailed analysis, the 10 most common NSAIDs and clinical departments were evaluated. In addition, data on the concomitant use of RAAS blockers and lithium (ATC code: A02B2) were extracted. RAAS blockers were defined as angiotensin II receptor blockers (ARB, ATC code: C09C), angiotensin-converting-enzyme inhibitors (ACE-I, ATC code: C09A), direct renin inhibitors (ATC code: C09X), and aldosterone receptor antagonists (ATC code: C03A1).

Patients with CKD were identified during the observation and screening periods from the diagnostic fields using the International Classification of Diseases, 10th Revision

(ICD-10). We collected information about CKD grade as follows: CKD not classified by stage (ICD-10 code: N289, N189) and CKD stages 3–5 (ICD-10 code: N188, N180). Among the patients with ICD-10 code of N289, CKD stages 1 and 2 (determined by text code) were assessed as non-CKD. In addition, patients who underwent dialysis and those with missing data were excluded. Dialysis was defined using the standard clinical practice text that included dialysis and/or peritoneal dialysis. Moreover, data of patient age, sex (male/female), and duration of NSAID use (in regular use patients) were collected. Prescription durations were calculated as the total number of prescription days. If there was more than 1 week between the prescription end date and the next prescription start date, it was determined as the end of administration.

Outcomes

First, we evaluated the proportions of CKD diagnosis and NSAID prescription by different clinical departments and institutions (e.g., CKD was diagnosed by the internal medicine department, NSAIDs were prescribed by another department).

Second, in patients with CKD, the five most frequent combination patterns of clinical departments that prescribed NSAID and diagnosed CKD were evaluated. Moreover, in each combination pattern, the proportions of CKD diagnosis and NSAID prescription by

different clinical institutions were calculated.

Third, the proportions of occasional or regular use of NSAIDs, concomitant use of lithium and RAAS blockers, and duration of regular use of NSAIDs were compared between the CKD and non-CKD groups. We also examined patient characteristics, including patient age, sex (male/female), the 10 most frequently prescribed NSAIDs and clinical departments prescribing NSAIDs. To evaluate the duration of NSAID administration, we added two groups: (1) patients with CKD with prescription and diagnosis from the same department (same departments group) and (2) patients with CKD with prescription and diagnosis from different departments (different departments group).

Finally, among the enrolled patients for the secondary analysis (i.e., adult patients who were diagnosed with CKD during the observation and screening periods), the proportion of NSAID prescriptions during the observation period was calculated.

Data analyses

Mann–Whitney U test was employed to compare the continuous variables (all continuous variables had non-normal distributions). Categorical variables were compared using Pearson's chi-square or Fisher's exact test. Fisher's exact test was employed when more than 20% of cells had expected frequencies of <5 [13]. A P value ≤0.05 was considered

to indicate statistical significance. JMP 14® (SAS Institute Inc., Cary, NC, USA) was employed for all statistical analyses.

Ethics

The institutional review board of the Faculty of Pharmaceutical Sciences of Hokkaido University waived the requirement for informed consent because of the anonymous nature of the data.

RESULTS

Patient characteristics

As shown in Figure 1, 224 014 patients were included in the study and classified into the CKD (n = 1501) and non-CKD groups (n = 222 513). In the CKD group, CKD was classified as stage 3 (n = 12), stage 3A (n = 15), stage 3B (n = 6), stage 4 (n = 8), stage 5 (n = 2), stage 5D (n = 0), and unclassified (n = 1460). Among these patients, two had duplicate registrations. Generally, CKD stage 3 is classified into stages 3A and 3B [6]. In the JMDC claims database, cases with CKD stages 3, 3A, and 3B were registered individually (i.e., some cases were registered as CKD stage 3, whereas some were

registered as stage 3A or 3B). Therefore, the sum of patients with CKD stage 3A (n = 15) and stage 3B (n = 6) was different from the number of patients with stage 3 (n = 12). In addition, 15 patients with CKD stages 1 (4 patients) and 2 (11 patients) were assessed as those without CKD.

The patient characteristics are shown in Table 1. Patients in the CKD group were older than those in the non-CKD group, and a higher proportion was male. Loxoprofen sodium hydrate was the most frequently prescribed NSAID in all groups, whereas, the prescription proportion of loxoprofen sodium hydrate and ibuprofen was higher in the non-CKD group than in the CKD group. The prescription proportion of celecoxib and etodolac (selective COX-2 inhibitors) was higher in the CKD group than in the non-CKD group.

Proportions of CKD diagnosis and NSAID prescription by clinical departments and institutions

Table 2 shows details of the departments that diagnosed CKD and prescribed NSAIDs. The internal medicine departments diagnosed the majority of patients with CKD (74.8%) but only 50.4% of the patients were prescribed NSAIDs by this department. NSAIDs were often prescribed by orthopedic surgery departments (20.4% of the patients), although

there were relatively few diagnoses of CKD (1.73%) by these departments.

As shown Figure 2, among the patients with CKD (n = 1501), 50.4% patients received CKD diagnosis and NSAID prescription from different clinical departments; and 72.8% received from different medical institutions.

Figure 3 shows the five most frequent combination patterns of clinical departments that prescribed NSAIDs and diagnosed CKD. The internal medicine department most often prescribed NSAIDs and diagnosed CKD (Pattern A). However, in this pattern, 51.1% of the patients were prescribed NSAIDs by clinical institutions that were different from those that diagnosed CKD. In the other patterns (Patterns B, C, D, and E), all NSAIDs were prescribed by departments and institutions that were different from those that diagnosed CKD.

Comparison of usage of NSAIDs and concomitant medications

Table 3 shows details of NSAID usage and concomitant medications. The proportions of regular NSAID use and concomitant use of all RAAS blockers were higher in the CKD groups than in the non-CKD group.

For patients regularly using NSAIDs, the duration of use was evaluated in four groups (Figure 4). Although the standard deviations for the groups varied widely, the average

duration was the longest in the same departments group and shortest in the different departments group.

Proportion of NSAID prescription for patients with CKD

For the secondary analysis, the proportion of NSAID prescription for patients with CKD was evaluated. During the observation and screening periods (January 2014 to March 2016), 89 336 patients were diagnosed with CKD. Among these patients, those aged <20 years (n = 17), with stages 1 and 2 CKD (n = 233), and who underwent dialysis (n = 1937) were excluded, and finally, 87 149 patients were enrolled. Thus, 1.72% patients (1501 patients out of the 87 149) with CKD were newly prescribed oral NSAIDs from January 2016 to March 2016 (observation period) in the out-patient department.

DISCUSSION

In this study, we attempted to elucidate the current situation regarding CKD diagnosis and NSAID prescription by different clinical departments and patterns of NSAID usage by patients with CKD compared with those without CKD.

Of the 224 014 patients enrolled in the study, 1501 were identified to be diagnosed with CKD; however, most of these patients were not classified into one of the CKD stages in

the JMDC claims database. Thus, the CKD group might consist of patients for whom NSAID use is not restricted, such as CKD stages 1 and 2. This is a major limitation of this study. In addition, patients who underwent dialysis were excluded in this study, because it is not necessary to consider renal toxicity of NSAIDs for patients who already underwent dialysis. However, it is important for future studies to investigate the prescription status of NSAIDs especially before the initiation of dialysis [14].

Loxoprofen sodium hydrate was the most commonly prescribed NSAID in the two groups (Table 1), which is consistent with the finding of a previous study [15]. The prescription proportions of celecoxib and etodolac (selective COX-2 inhibiters) were higher in the CKD group than in the non-CKD group. However, there is no evidence that COX-2 inhibitors suppress the development of CKD and the KDIGO guidelines [5] warn against using NSAIDs with COX-2 inhibitors.

As shown in Table 2, the internal medicine departments diagnosed CKD most frequently (74.8% of the patients), whereas surgical departments rarely diagnosed CKD. In addition, as shown in Figure 2, more than half of the patients received CKD diagnosis and NSAID prescription from different clinical departments and medical institutions. Although the internal medicine department most often prescribed NSAIDs and diagnosed CKD (Figure 3; Pattern A), 51.1% of these patients were prescribed NSAIDs by clinical

institutions that were different from those that diagnosed CKD. In addition, in the other patterns (Patterns B, C, D, and E), all NSAIDs are prescribed by departments and institutions that were different from those that diagnosed CKD. Thus, these patterns indicate that CKD was mostly diagnosed by the internal medicine departments, whereas NSAIDs were often prescribed by other departments and institutions. However, we cannot conclude that these results are inappropriate. In this study, the CKD stage was not known for most patients but the prescribing clinician may have evaluated the CKD stage even if the department or institution of diagnosis was different. However, considering only out-patients were enrolled in this study, it is possible that NSAIDs are being prescribed to patients with CKD without the advice or input from the clinicians who diagnosed them.

The proportion of regular NSAID use was higher in the CKD groups than in the non-CKD group (Table 3), and the average duration of use tended to be longer for patients who received a diagnosis and prescription from the same clinical department (40.2 d, Figure 4). In other words, clinicians who diagnose CKD may be advising long-term NSAID administration for complications such as rheumatoid arthritis [16]. The concomitant use of RAAS blockers, especially ARB, was more common in patients with CKD than in those without CKD. ARBs are widely prescribed for patients with CKD because they

delay CKD progression [17-19]. However, the concomitant use of NSAIDs and ARBs is not recommended in the KDIGO guidelines [5]. There was no difference in the duration of use between patients with CKD and those without CKD, despite the fact that short-term use is recommended for patients with CKD [5]. These results suggest that NSAIDs are being prescribed inappropriately for patients with CKD in Japan. However, as described above, it is possible that these results were due to prescriptions for which either long-term duration was judged possible based on CKD grade, or CKD was not considered. Thus, resolving this question should be a priority for future studies.

The secondary analysis revealed that 1.72% patients with CKD were newly prescribed oral NSAIDs during the observation period in the out-patient department. This proportion was also lower than that reported previously [7-9]. This can be attributed to the following reasons: (1) the enrolled patients were <75 years of age, (2) the observation period (i.e., January 2016 to March 2016) was relatively short, and (3) the usage of over-the-counter medication was not evaluated [7-9].

Our study had some limitations. First, the JMDC claims database includes only company employees and their family members (<75 years of age). Therefore, we were not able to evaluate elderly patients. Second, the accuracy of CKD diagnosis, that is, their ICD-10 codes could not be evaluated. Third, we judged regular or occasional use of

NSAIDs based on prescription. In addition, the duration of NSAID use was calculated as the total number of prescription days. However, as NSAIDs are self-administered by patients, the actual use could not be evaluated.

In summary, our study revealed the possibility that NSAIDs are prescribed without advice or input from the clinicians who diagnosed CKD and, therefore, it is possible that these drugs are being prescribed inappropriately in Japan. We believe this new finding is important for clinicians and pharmacists. In addition, the progression of CKD can lead to renal replacement therapy, and the older individuals are known to be at risk [5,6,20]. In 2019, Japan's aging proportion (the ratio of the population aged 65 and older to the total population) exceeded 25%, ahead of any other country in the world [21]. For the prevention of CKD progression, our novel approach of examining differences in the clinical departments that provide diagnosis and prescription is meaningful, because it can be applied to other renal toxic medications and developed further. Clinicians who diagnose CKD must pay attention to concomitant medications, especially those prescribed by other clinical departments. In addition, clinicians who prescribe NSAIDs must consider the medical history of patients, as should pharmacists who dispense the medications.

CONCLUSION

Our study revealed that NSAIDs are often prescribed to patients with CKD from different clinicians than those who diagnosed them. Thus, NSAIDs are potentially being prescribed inappropriately for patients with CKD in Japan.

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None.

CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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Tables

Table 1. Comparison of patient characteristics

Description	CKD group (n = 1501)	Non-CKD group (n = 222 513)	*P* value
Age (years), median (IQR)	52 (44–59)	43 (34–52)	<0.001*
Sex (male), n (%)	924 (61.6)	124 480 (55.9)	<0.001*
Sex (female), n (%)	577 (38.4)	98 033 (44.1)	
NSAIDs (ATC code: M01A1 and M01A3), n (%)			
Loxoprofen sodium hydrate	1009 (67.2)	157 858 (70.9)	0.0016*
Ibuprofen	59 (3.93)	12 532 (5.63)	0.0043*
Diclofenac sodium	85 (5.66)	11 611 (5.22)	0.4460
Celecoxib	126 (8.39)	10 922 (4.91)	<0.001*
Mefenamic acid	31 (2.07)	6115 (2.75)	0.1065
Tiaramide hydrochloride	42 (2.80)	5463 (2.46)	0.3923
Pranoprofen	24 (1.60)	4256 (1.91)	0.3762
Etodolac	34 (2.27)	3122 (1.40)	0.0047*
Lornoxicam	26 (1.73)	3068 (1.38)	0.2423
Zaltoprofen	21 (1.40)	2669 (1.20)	0.4792
Other NSAIDs	44 (2.93)	4897 (2.20)	0.0548

* The results with *P* values of ≤0.05 were considered statistically significant. IQR: inter quartile range, CKD: chronic kidney disease, NSAIDs: nonsteroidal anti-inflammatory drugs. Mann–Whitney U test was used to compare the continuous variables. Categorical variables were compared using Pearson’s chi-square or Fisher’s exact test. Fisher's exact test was employed when more than 20% of cells had expected frequencies of <5.

Table 2. Details of the departments that diagnosed CKD and prescribed NSAIDs.

Description	CKD group (n = 1501)	Non-CKD group (n = 222 513)	*P* value
Clinical departments of prescription, n (%)			
Internal medicine	757 (50.4)	110 388 (49.6)	0.5249
Orthopedic surgery	306 (20.4)	39 785 (17.9)	0.0116
Otorhinolaryngology	103 (6.86)	23 045 (10.4)	<0.001*
General surgery	57 (3.80)	9285 (4.17)	0.4685
Gastroenterology	19 (1.27)	4215 (1.89)	0.0748
Obstetrics and gynecology	8 (0.53)	2623 (1.18)	0.0206*
Dermatology	16 (1.07)	3372 (1.52)	0.1550
Pediatrics	8 (0.53)	3300 (1.48)	0.0024*
Neurosurgery	21 (1.40)	2795 (1.26)	0.6203
Respiratory medicine	16 (1.07)	1449 (0.65)	0.0469*
Other clinical departments	190 (12.7)	22 256 (10.0)	<0.001*
Clinical departments of CKD diagnosis, n (%)			
Internal medicine	1122 (74.8)	-	-
Orthopedic surgery	26 (1.73)	-	-
Otorhinolaryngology	2 (0.13)	-	-
General surgery	29 (1.93)	-	-
Gastroenterology	26 (1.73)	-	-
Obstetrics and gynecology	2 (0.13)	-	-
Dermatology	2 (0.13)	-	-
Pediatrics	4 (0.27)	-	-
Neurosurgery	16 (1.07)	-	-
Respiratory medicine	30 (2.00)	-	-
Other clinical departments	242 (16.1)	-	-

*The results with *P* values of ≤0.05 were considered significant. CKD: chronic kidney disease, NSAIDs: nonsteroidal anti-inflammatory drugs. Variables were compared using Pearson’s chi-square or Fisher’s exact test. Fisher's exact test was employed when more than 20% of cells had expected frequencies of <5.

Table 3. Comparison of usage of NSAIDs and concomitant medications.

Description	CKD group (n = 1501)	Non-CKD group (n = 222 513)	*P* value
Regular NSAID use, n (%)	1070 (71.3)	150 786 (67.8)	0.0036*
Occasional NSAID use, n (%)	431 (28.7)	71 727 (32.2)	
Concomitant medications, n (%)			
Lithium (ATC code: A02B2)	6 (0.40)	574 (0.26)	0.2814
RAAS blockers (ATC code: C09C, C09A, C09X and C03A1)	515 (34.3)	18 114 (8.14)	<0.001*
Angiotensin II receptor blockers (ATC code: C09C)	476 (31.7)	16 743 (7.52)	<0.001*
Angiotensin-converting enzyme inhibitors (ATC code: C09A)	39 (2.60)	1209 (0.54)	<0.001*
Direct Renin Inhibitors (ATC code: C09X)	3 (0.20)	40 (0.02)	0.0030*
Aldosterone receptor antagonists (ATC code: C03A1)	36 (2.40)	677 (0.30)	<0.001*

*The results with *P* values of ≤ 0.05 were considered significant. CKD: chronic kidney disease, NSAID: nonsteroidal anti-inflammatory drug, RAAS: renin-angiotensin-aldosterone system. Variables were compared using Pearson’s chi-square or Fisher’s exact test. Fisher's exact test was employed when more than 20% of cells had expected frequencies of <5.

Figure legends

Figure 1. Flowchart of patients included in a study of NSAID prescriptions in Japan.

CKD: chronic kidney disease, NSAID: nonsteroidal anti-inflammatory drug. Fifteen patients with stages 1 (4 patients) and 2 (11 patients) CKD were assessed as non-CKD.

Figure 2. Proportions of NSAID prescription and CKD diagnosis by different clinical departments and institutions.

CKD: chronic kidney disease, NSAID: nonsteroidal anti-inflammatory drug.

Figure 3. Five most frequent combination patterns of clinical departments that prescribed NSAIDs and diagnosed CKD.

CKD: chronic kidney disease, NSAID: nonsteroidal anti-inflammatory drug. “Proportions of different institutions” means proportions of CKD diagnosis and nonsteroidal anti-inflammatory drug prescription by different clinical institutions in each pattern.

Figure 4. Comparison of average durations of NSAID use.

NSAID: nonsteroidal anti-inflammatory drug; data are shown as average and standard

deviation.

Fig. 1

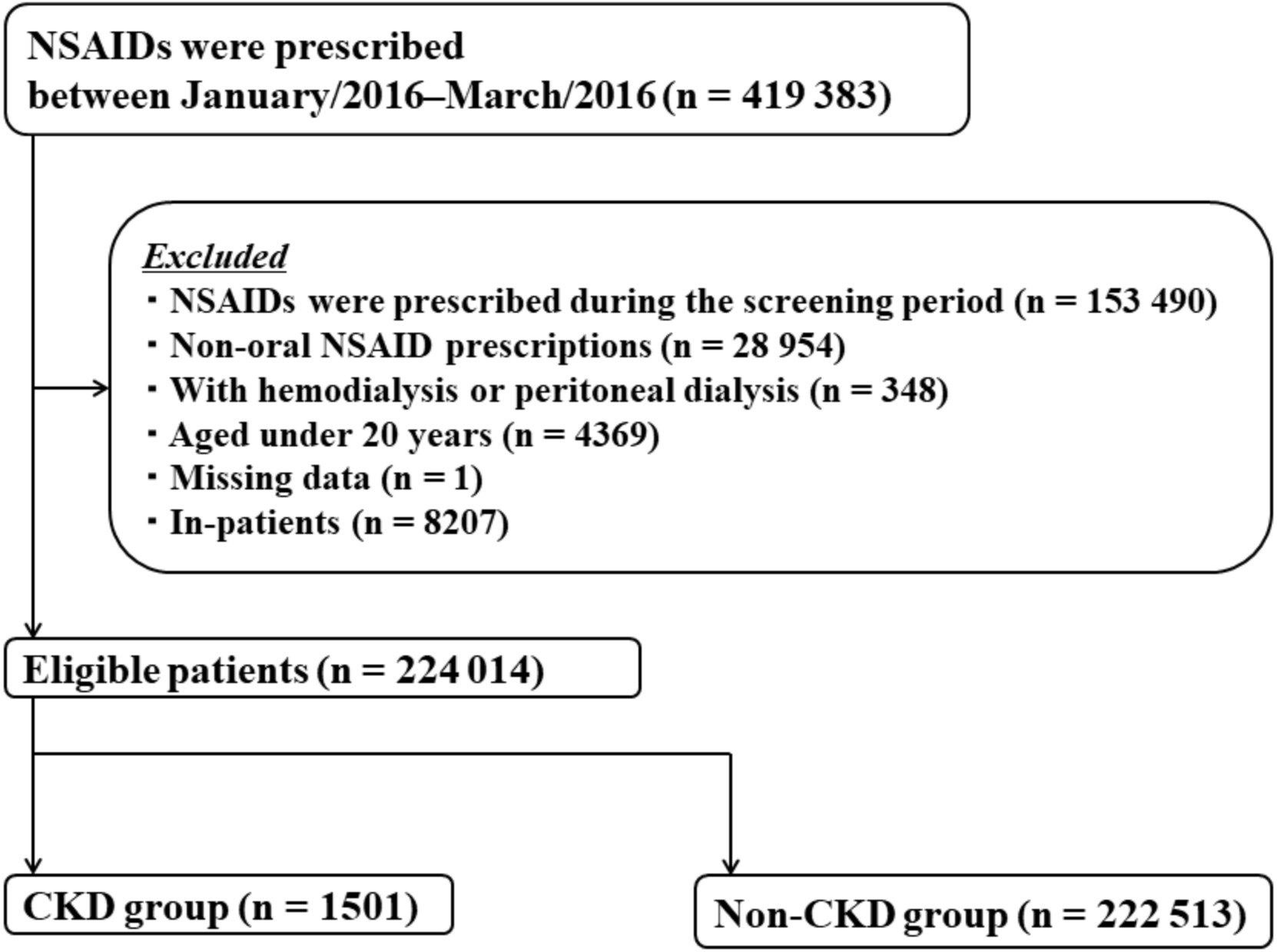
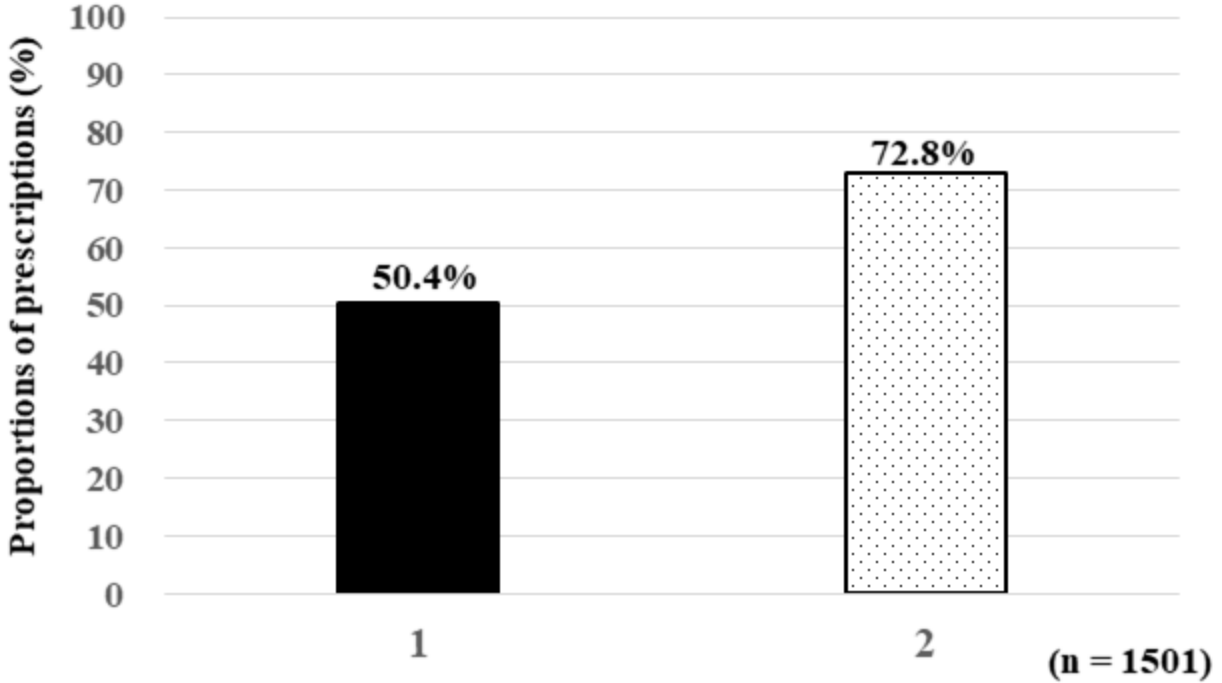
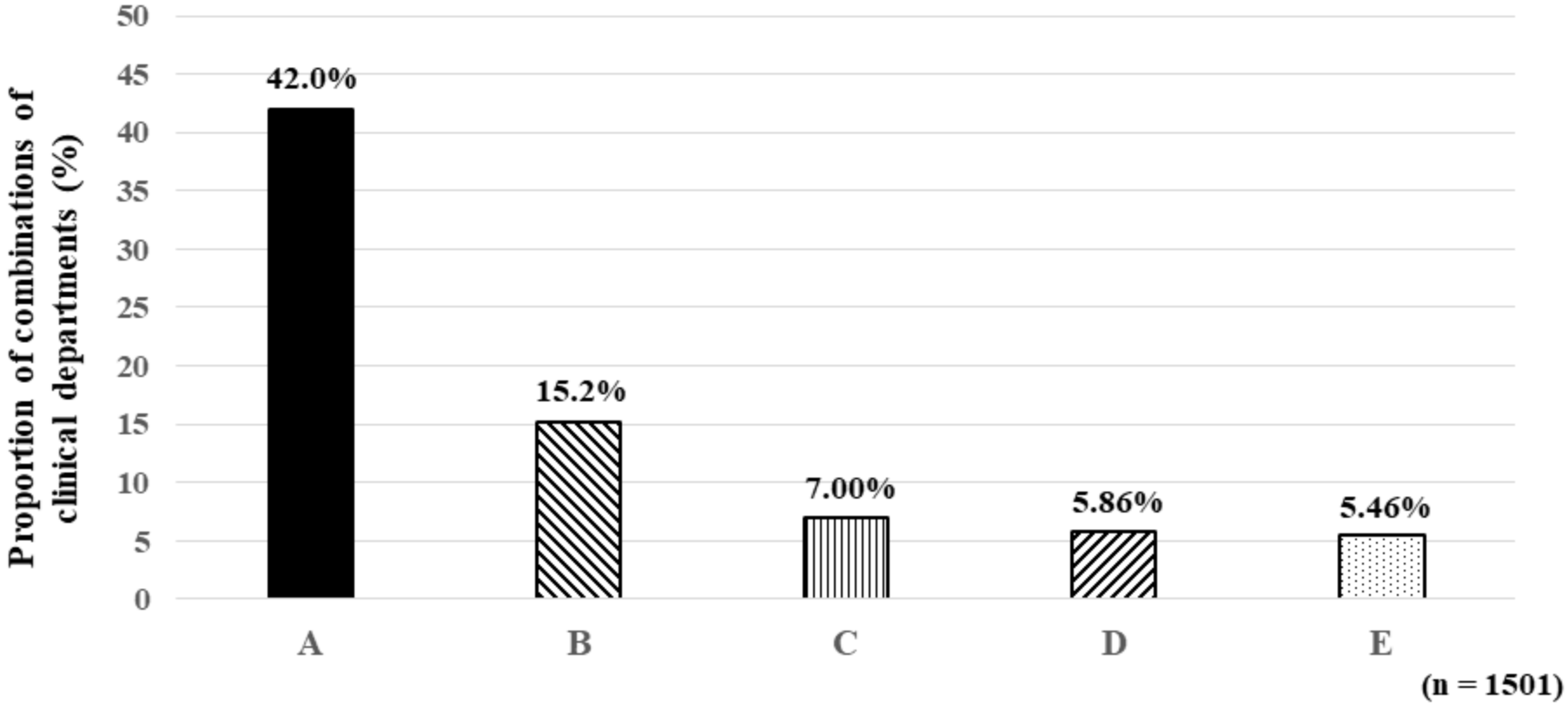

NSAIDs were prescribed
between January/2016–March/2016 (n = 419 383)
Excluded
・NSAIDs were prescribed during the screening period (n = 153 490)
・Non-oral NSAID prescriptions (n = 28 954)
・With hemodialysis or peritoneal dialysis (n = 348)
・Aged under 20 years (n = 4369)
・Missing data (n = 1)
・In-patients (n = 8207)
Eligible patients (n = 224 014)
CKD group (n = 1501)
Non-CKD group (n = 222 513)

Fig. 2



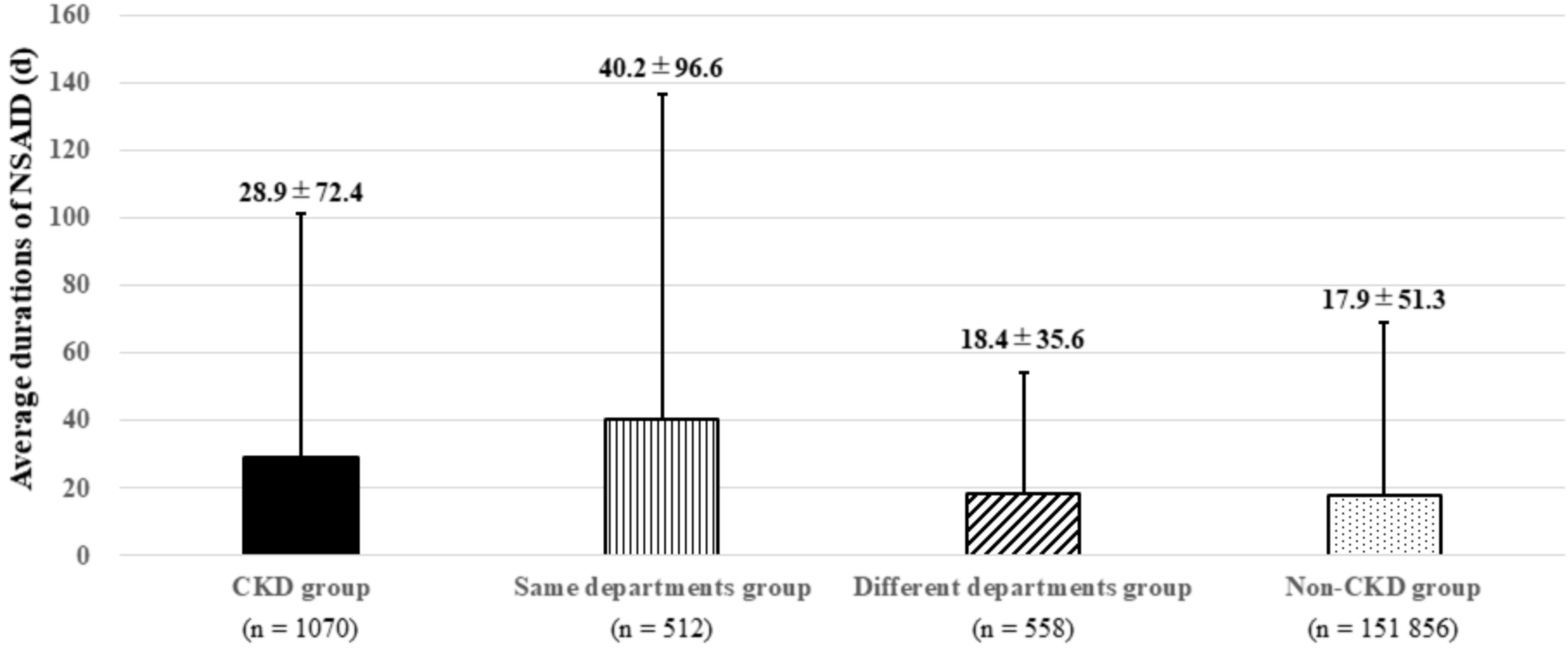
Patterns	n	NSAID prescription and CKD diagnosis
1	756	Clinical department differed between prescription and diagnosis
2	1,092	Medical institution differed between prescription and diagnosis

Fig. 3



Patterns	n	Clinical departments of prescriptions and diagnosis		Proportions of different institutions
		Prescriptions of NSAID	Diagnosis of CKD	
A	630	Internal medicine	Internal medicine	51.1 %
B	228	Orthopedic surgery	Internal medicine	100 %
C	105	Other clinical departments	Internal medicine	100 %
D	88	Internal medicine	Other clinical departments	100 %
E	82	Otorhinolaryngology	Internal medicine	100 %

Fig. 4


Average durations of NSAID (d)
160
140
120
100
80
60
40
20
0
28.9 ± 72.4
40.2 ± 96.6
18.4 ± 35.6
17.9 ± 51.3
CKD group
(n = 1070)
Same departments group
(n = 512)
Different departments group
(n = 558)
Non-CKD group
(n = 151 856)