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Community pharmacists' measurement of health-related quality of life in outpatients taking high-risk drugs

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Patients experiencing severe side effects when taking high-risk drugs may have a significantly reduced health-related quality of life (QOL); therefore, it is important to identify changes in the health-related QOL in these patients. This study aimed to determine the health-related QOL in community pharmacy outpatients taking high-risk drugs. This prospective observational study was conducted in 29 community pharmacies with 71 pharmacists in 12 regions and cities in Japan from October to December 2020 and 760 patients were enrolled. Using descriptive questionnaires of EuroQOL-5-dimensions-5-levels (EQ-5D-5L), community pharmacists obtained health-related QOL data from outpatients taking high-risk drugs. The mean health-related QOL of all outpatients was 0.869. The health-related QOL decreased with increasing age. The outpatient health-related QOL was 0.700, 0.763, 0.785, and 0.817 when taking antiepileptic, antidepressant, digitalis, and antiarrhythmic drugs, respectively, which was lower than the average health-related QOL of all outpatients. Mobility and pain/discomfort accounted for a large proportion of the decline in the health-related QOL with increasing age. There were no significant differences in personal care with increasing age; however, the number of outpatients with mobility, normal activity, and pain challenges decreased with age. In contrast, outpatients aged <65 years with anxiety/depression showed a lower than overall average health-related QOL. To the best of our knowledge, this is the first study in Japan to report an investigation by community pharmacists regarding health-related QOL assessment in outpatients taking high-risk drugs.

1. Introduction

Recent progress in the development and availability of new drugs has allowed many patients to receive medical treatment in an outpatient setting. Besides the benefits, all drugs have adverse effects; however, high-risk drugs require special management by the Ministry of Health, Labor, and Welfare in Japan. High-risk drugs comprise those: (i) that have a narrow therapeutic range, (ii) whose control of the administration method and dosage is challenging owing to the closeness between addiction and effectiveness, (iii) that have high individual differences in pharmacokinetics, (iv) that have high individual differences due to physiological factors (e.g., liver and kidney disorders and physiological differences in older adult patients and children), and (v) whose improper administration causes serious harm to patients. Furthermore, high-risk drugs comprise those in which medical accidents and incidents have been reported.

Many drugs, such as anticancer, anticoagulant, and antidiabetic drugs are established high-risk drugs that require pharmacological management at community pharmacies. When patients are taking high-risk drugs develop severe side effects, their quality of life (QOL) may be significantly reduced. Inappropriate prescription of drugs regarding adverse events led to a reduced QOL in the elderly (Wallace et al. 2016). For children, the QOL was similarly

reduced (Del Pozzo-Magana et al. 2015). Therefore, it is important to identify changes in QOL among those taking high-risk drugs. A health-related QOL scale can be used regardless of the disease or drug. Two methods for the scoring health-related QOL have been reported, profile-type and utility-value scales (Kuwahara et al. 2015). There are two methods for measuring the utility value: direct and indirect measurement methods. The EuroQol instrument was developed by an inter-disciplinary five-country group between 1987 and 1991; the EuroQol 5-dimensions-3-levels (EQ-5D-3L) is a tool used for indirect measurement (Devlin and Brooks 2017). After the development of EQ-5D-3L, the EuroQol-5-dimensions-5-levels (EQ-5D-5L) was developed. The five dimensions comprise mobility, personal care, usual activities, pain/discomfort, and anxiety/depression. The five levels are represented as 1, "no problems"; 2, "slight problems"; 3, "moderate problems"; 4, "severe problems", and 5, "unable." Participant responses are converted into a single preference-based score (i.e., a utility value), in which 0 indicates death, and 1 indicates perfect health, based on the Japanese value set. The EQ-5D-3L and EQ-5D-5L are widely used in many countries, and especially in Europe. A scoring method for the Japanese version of the EQ-5D-5L has been developed, which enables the health-related QOL to be evaluated in Japan based on the EQ-5D-5L (Herdman et al. 2011; Ikeda et al. 2015; Shirowa et al. 2016).

As the Japanese universal health care system covers all Japanese citizens (Ikegami and Campbell, 1995), assessing the health-related QOL using the EQ-5D can be an important tool in determining the economic evaluation of health technology in the country (Husereau et al. 2013). The health-related QOL can be measured in phase III clinical trials (Fukuda et al. 2013). Clinical hospital pharmacists in Japan have previously reported the results of measuring the outpatient health-related QOL (Hirose et al. 2020; Tanaka et al. 2019); however, a long-term patient QOL assessment has not been performed. Long-term QOL can be measured with the help of community pharmacists. These professionals provide long-term patient drug management, yet there have been few community pharmacy-based reports concerning the health-related QOL regarding community pharmacy outpatients taking high-risk drugs. Measurement of the patient health-related QOL by community pharmacists may lead to an enhanced understanding of the QOL in a real-world setting. This prospective observational study aimed to determine the health-related QOL of community

pharmacy outpatients taking high-risk drugs. To the best of our knowledge, the QOL of outpatients taking high-risk drugs has not been clarified so far.

2. Investigations and results

2.1. Outpatients

The characteristics of the study population are summarized in Table 1. During the survey period, 760 outpatients were enrolled in the study (average age, 68.5 years; men, n = 420 [55.3%]; women, n = 340 [44.7%]). The proportion of outpatients aged >65 years, who are considered older adults in Japan, was 68.2%. The proportion of outpatients >75 years, who require more care, was 35.8%. In total, 760 outpatients were taking an average of four drugs.

The most common high-risk drugs were anticoagulant (272 outpatients, 35.8%), anticancer (260 outpatients, 34.2%), and antidiabetic (236 outpatients, 31.1%) drugs.

2.2. Health-related QOL

The mean health-related QOL value concerning all 760 outpatients was 0.869. The mean health-related QOL value for each outpatient is shown in Table 2.

Table 1: Patient characteristics

	n = 760	%
Age (years)		
Average	68.5	
Median (range)	71 (22–95)	
Age stratification (years)		
<65	242	31.8%
65–69	85	11.2%
70–74	161	21.2%
75–79	129	17.0%
≥80	143	18.8%
Sex		
Male	420	55.3%
Female	340	44.7%
Family structure		
Living with others	163	21.4%
Living alone	30	3.9%
Not known	567	74.6%
The nursing insurance system		
Yes	15	2.0%
No	194	25.5%
Unknown	551	72.5%
Number of drugs		
Average	4	
Median (range)	3 (1–21)	
High-risk drugs		
Anticoagulant drugs	272	35.8%
Anticancer drugs	260	34.2%
Antidiabetic drugs	236	31.1%
Arrhythmia drugs	45	5.9%
Immunosuppressive drugs	43	5.7%
Psychiatric drugs	37	4.9%
Pancreatic hormones (Insulin)	31	4.1%
Antiepileptic drugs	9	1.2%
Theophylline	5	0.7%
Digitalis	4	0.5%
Anti-human immunodeficiency virus drugs	1	0.1%
Potassium	0	0%

Table 2: Health-related quality of life

	n	Health-related quality of life (average [95% confidence interval])
All patients	760	0.869 (0.858–0.880)
Sex		
Male	420	0.881 (0.867–0.896)
Female	340	0.853 (0.836–0.870)
Age stratification (years)		
<65	242	0.889 (0.871–0.906)
65–69	85	0.879 (0.845–0.912)
70–74	161	0.875 (0.851–0.898)
75–79	129	0.862 (0.833–0.891)
≥80	143	0.829 (0.801–0.856)
Family structure		
Living with others	163	0.850 (0.821–0.878)
Living alone	30	0.787 (0.715–0.859)
The nursing insurance system^a		
Yes	15	0.774 (0.636–0.911)
No	194	0.876 (0.855–0.896)
High-risk drugs		
Anticoagulant drugs	272	0.871 (0.853–0.889)
Anticancer drugs	260	0.871 (0.854–0.889)
Antidiabetic drugs	236	0.879 (0.859–0.899)
Arrhythmia drugs	45	0.817 (0.758–0.876)
Immunosuppressive drugs	43	0.844 (0.789–0.900)
Psychiatric drugs	37	0.763 (0.705–0.821)
Pancreatic hormones (Insulin)	31	0.835 (0.785–0.910)
Antiepileptic drugs	9	0.700 (0.495–0.906)
Theophylline	5	0.865 (0.652–1.077)
Digitalis	4	0.785 (0.358–1.211)
Anti-human immunodeficiency virus drugs	1	0.823

^aPersons aged ≥65 years can receive support regardless of the cause when they need support or nursing care. People aged 40–64 years can receive support when they need support or care due to diseases such as cancer or rheumatoid arthritis.

The health-related QOL values were lower in women (0.853) than in men (0.881). The health-related QOL of outpatients aged 40 to 64 years (in the group of nursing insurance-Yes), who needed assistance, and that of outpatients aged ≥65 years (in the group of nursing insurance-No) were lower than those among the other age groups.

The health-related QOL values according to age were as follows: outpatients aged <65 years, 0.889; outpatients aged 65–69 years, 0.879; outpatients aged 70–74 years, 0.875; outpatients aged 75–79 years, 0.862, and outpatients aged >80 years, 0.829.

Older outpatients had a lower health-related QOL, with outpatients aged >80 years having the lowest health-related QOL.

Health-related QOL values according to high-risk drugs were as follows: antidiabetic drugs, 0.879; anticoagulant drugs, 0.871; and anticancer drugs, 0.871; all exceeded the average health-related QOL value (0.869) for all outpatients. However, the health-related QOL was 0.700 for those taking antiepileptic drugs, 0.763 for those taking antidepressant drugs, 0.785 for those taking digitalis,

and 0.817 for those taking antiarrhythmic drugs; these values were lower than the average health-related QOL value for all outpatients. The health-related QOL of 163 patients who did not live alone was 0.850 and 0.787 for 30 patients who lived alone.

2.3. Values using 5-dimensions-5-levels according to age groups

Health-related QOL values according to age groups are shown in the Fig. The EQ-5D-5L consists of five dimensions and five levels. Pain/discomfort had the lowest proportion among all 760 outpatients. Mobility and pain/discomfort accounted for a large proportion of the decline in health-related QOL with increasing age. There was no difference in personal care according to age; however, in terms of mobility, normal activity, and pain, the number of outpatients with no problems decreased with age. In contrast, anxiety showed the lowest proportion among those aged <65 years with no health-related QOL difficulties.

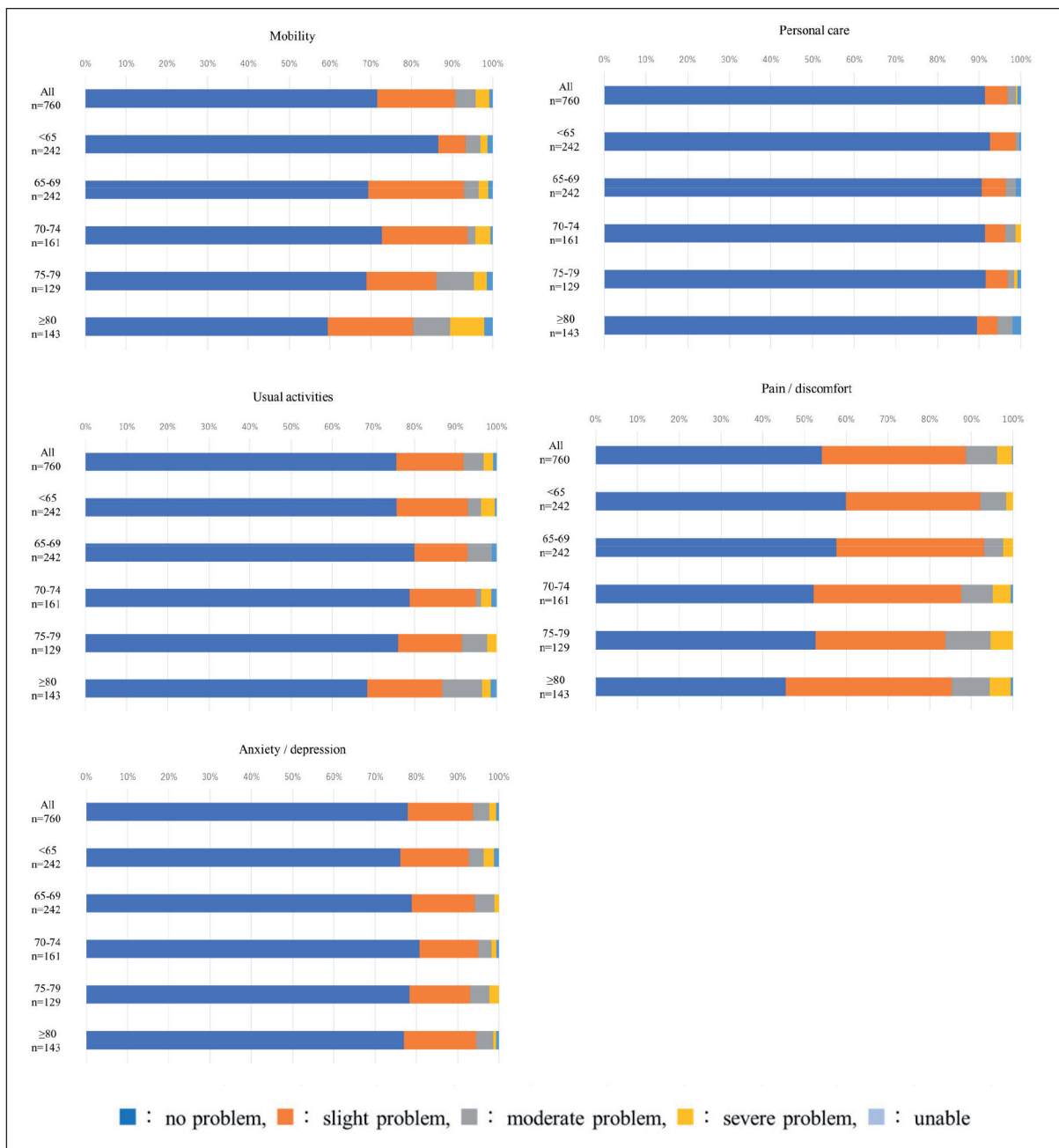


Fig.: Each value by 5-dimensions-5-levels according to the age group

3. Discussion

We determined the health-related QOL in community pharmacy outpatients taking high-risk drugs in Japan. This is the first study in Japan to report an investigation by community pharmacists on the health-related QOL assessment in outpatients taking high-risk drugs.

It has been reported that the health-related QOL of the Japanese general population is 0.877 (instrument: EQ-5D-3L) (Fujikawa et al. 2011). The health-related QOL in this study was 0.869, which is similar to findings from previous inpatient studies (Fujikawa et al. 2011), and our findings and those of previous studies are in general agreement. We consider that advances in supportive care can help explain why the health-related QOL does not decline in patients with terminal cancer. Furthermore, the possibility of taking oral anticoagulants directly may also explain why the health-related QOL of patients taking antithrombotic drugs did not decrease. The health-related QOL of diabetic patients in this study was 0.879 and did not decline, which is similar to findings of previous studies in Japan (Takahara et al. 2019). The presence or absence of diabetic complications may have a significant impact on the QOL.

However, the health-related QOL of patients taking antiepileptic, antidepressant, and cardiotonic drugs was low, which may have been due to patient anxiety levels. Acceptance of death is one of the stages in patients with cancer, as proposed in Kubler-Ross's five stages of death (Oransky 2004), which may explain the reduced levels of anxiety. In the case of other diseases, it is necessary to research how patients accept their diagnosis and determine the subsequent implications for the QOL.

The health-related QOL relating to the five dimensions of mobility, personal care, usual activities, pain/discomfort, and anxiety/depression was determined for community pharmacy outpatients taking high-risk drugs; this evaluation was related to the effects of each factor on the health-related QOL. To our knowledge, no previous studies have reported such findings. When focusing on the health-related QOL according to age group, we expected that the mobility dimension would show a decline with age. However, anxiety/depression showed a lower than average health-related QOL in those aged <65 years. Young outpatients might be anxious about their illnesses and about how to spend the rest of their lives. The relation of this to the QOL of young outpatients, however, is unclear. This study revealed the EQ-5D-5L dimensions that contributed to a lower health-related QOL according to age, which may help community pharmacists manage outpatient interventions in the future.

This study had some limitations. First, the participants were outpatients who had agreed to participate in this prospective observational study; therefore, it is likely that collaborating patients with a good health-related QOL were enrolled, which may have resulted in a selection bias. Furthermore, patients who interact more readily with the pharmacists may have been selected, which could have further contributed to the selection bias. Second, this study did not consider the duration of high-risk drug administration—some patients might have just started high-risk drug treatments, whereas others might have been taking high-risk drugs for a long time. The duration of treatment may have affected the health-related QOL. For patients with cancer, their psychological stage (denial, anger, bargaining, depression, and acceptance) at the time of the questionnaire may have influenced their responses. However, for patients with non-cancer diseases, the duration of drug administration may be a factor affecting the health-related QOL of the patient. Although treatment duration was not investigated in this study, it may be an important factor.

This exploratory study was the first study wherein community pharmacists determined the health-related QOL of outpatients taking high-risk drugs. In the future, a new study will measure the health-related QOL four or more times to obtain more accurate values and propose a method that does not reduce the health-related QOL. Furthermore, we intend to provide an economic evaluation of health technology using the health-related QOL based on EQ-5D-5L.

4. Experimental

4.1. Study design and patients

A prospective observational study was undertaken at 29 community pharmacies with 71 pharmacists in 12 regions and cities (Tokyo, Kanagawa, Saitama, Chiba, Gunma, Tochigi, Hokkaido, Aichi, Osaka, Kagawa, Tokushima, and Fukuoka) in Japan from October to December 2020. Seventy-one community pharmacists measured the health-related QOL of outpatients using the EQ-5D-5L questionnaire. This process was conducted after obtaining informed consent from outpatients who had been prescribed high-risk drugs such as anticancer, immunosuppressive, arrhythmia, antiepileptic, anticoagulant, and digitalis drugs, along with theophylline and potassium; and psychiatric drugs, antidiabetic drugs, pancreatic hormones (insulin), and anti-human immunodeficiency virus drugs. The outpatients were aged ≥ 20 years. Community pharmacists confirmed the health-related QOL regardless of whether the prescription was the first, second, or repeat prescription. Outpatients were enrolled regardless of whether they had previously started treatment.

4.2. Measurement of the health-related QOL using EQ-5D-5L

Outpatients were asked to respond to the questionnaire during their waiting time. A paper form of the Japanese version of the EQ-5D-5L questionnaire was used (Herdman et al. 2011; Ikeda et al. 2015; Shiroiwa et al. 2016). The questionnaires were administered by community pharmacists and there was no remuneration for the participants. The community pharmacist who received the EQ-5D-5L questionnaire recorded the responses along with relevant medical data such as age, sex, drugs taken, drug adherence, and medical history. A EuroQol group (Rotterdam, The Netherlands) license was obtained for research purposes.

Trial registration: UMIN-CTR study design: trial number UMIN 000041942. Registered 30 September 2020, <https://www.umin.ac.jp>.

Ethics approval and consent to participate: The study was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committees of the School of Nursing and Rehabilitation Sciences, Showa University (Approval number: 528), and other participating centers. We obtained and archived written informed consent from all patients. Patient data was anonymized to protect their privacy.

Conflicts of interest: none declared.

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