

Prevalence and Factors Associated with Drug-Drug Interactions among Elderly Cancer Patients in a University Hospital

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Abstract

Objective: To investigate the prevalence, severity, and factors associated with drug-drug interactions (DDIs) among elderly cancer patients receiving chemotherapy. **Methods:** This retrospective cross-sectional study was conducted among 390 patients aged 65 years and older at Srinagarind Hospital between January 1 and December 31, 2023. The study retrieved medication data from electronic medical records and identified DDIs using information from the Lexicomp® database and the 2023 American Geriatrics Society (AGS) Beers Criteria®. **Results:** The prevalence of potential DDIs according to the Lexicomp® database was 97.4%, whereas potentially inappropriate drug combinations identified using the Beers Criteria® accounted for 23.8%. Multivariable logistic regression analysis identified factors significantly associated with the presence of potential DDIs based on the Lexicomp® database including concurrent use of ten or more medications (aOR 18.04, 95% CI: 6.05–53.86, $P < 0.001$), metastatic cancer stage (aOR 1.88, 95% CI: 1.18–3.00, $P = 0.008$), gynecologic malignancy (aOR 3.59, 95% CI: 1.65–7.80, $P = 0.001$) and other cancer types (aOR 5.26, 95% CI: 1.96–14.16, $P = 0.001$). Most DDIs were classified as Risk C interactions (56.5% of unique interacting drug pairs). **Conclusion:** Elderly cancer patients receiving chemotherapy demonstrated a high prevalence of potential DDIs. Number of medications received by patients was significantly associated with an increase in potential DDIs. Therefore, pharmacists should play an active role in systematically reviewing medication and monitoring potential DDIs in collaboration with a multidisciplinary healthcare team to enhance medication safety for patients.

Keywords: drug-drug interactions, polypharmacy, elderly cancer patients, chemotherapy

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ความชุกและปัจจัยที่สัมพันธ์กับการเกิดอันตรกิริยาระหว่างยา ในผู้ป่วยสูงอายุโรคมะเร็งในโรงพยาบาลมหาวิทยาลัยแห่งหนึ่ง

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บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาความชุก ความรุนแรง และปัจจัยที่สัมพันธ์กับการเกิดอันตรกิริยาระหว่างยา (drug-drug interactions: DDIs) ในผู้ป่วยสูงอายุโรคมะเร็งที่ได้รับยาเคมีบำบัด **วิธีการ:** การวิจัยเชิงพรรณนาภาคตัดขวางแบบย้อนหลังครั้ง
นี้ทำในผู้ป่วยอายุ 65 ปีขึ้นไปจำนวน 390 ราย ณ โรงพยาบาลศรีนครินทร์ ระหว่างวันที่ 1 มกราคม ถึง 31 ธันวาคม 2566
การศึกษาเก็บข้อมูลเกี่ยวกับยาจากฐานข้อมูลระเบียบประวัติอิเล็กทรอนิกส์ และประเมิน DDIs โดยใช้ข้อมูลจากฐานข้อมูล
Lexicomp® และ Beers Criteria® ฉบับปรับปรุงปี 2023 ของสมาคมผู้สูงอายุแห่งอเมริกา **ผลการวิจัย:** ความชุกของอันตรกิริยา
ระหว่างยาที่อาจเกิดขึ้น (potential DDIs) ตามฐานข้อมูล Lexicomp® เท่ากับร้อยละ 97.4 ความชุกของคู่ยาที่อาจไม่เหมาะสม
(potentially inappropriate drug combinations) ตาม Beers Criteria® เท่ากับร้อยละ 23.8 การวิเคราะห์ถดถอยโลจิสติกส์แบบ
พหุตัวแปรพบว่า ปัจจัยที่มีความสัมพันธ์อย่างมีนัยสำคัญกับการเกิด potential DDIs ตามฐานข้อมูล Lexicomp® ได้แก่ การใช้ยา
ร่วมกันตั้งแต่ 10 รายการขึ้นไป (aOR 18.04, 95% CI: 6.05–53.86, P<0.001) ระยะโรคมะเร็งที่มีการแพร่กระจาย (aOR 1.88,
95% CI: 1.18–3.00, P=0.008) มะเร็งทางนรีเวช (aOR 3.59, 95% CI: 1.65–7.80, P=0.001) และโรคมะเร็งชนิดอื่นๆ (aOR
5.26, 95% CI: 1.96–14.16, P=0.001) คู่ยาที่พบจาก DDIs ส่วนใหญ่มีความเสี่ยงระดับ C (ร้อยละ 56.5 ของคู่ยาที่พบ) **สรุป:**
ผู้ป่วยสูงอายุโรคมะเร็งที่ได้รับยาเคมีบำบัดมีความชุกในการเกิด potential DDIs สูง จำนวนรายการยาที่ผู้ป่วยได้รับมี
ความสัมพันธ์อย่างมีนัยสำคัญกับการเกิด potential DDIs ที่เพิ่มขึ้น เภสัชกรจึงควรมีบทบาทในการทบทวนรายการยาและเฝ้า
ระวังอันตรกิริยาระหว่างยาอย่างเป็นระบบร่วมกับทีมสหสาขาวิชาชีพ เพื่อเพิ่มความปลอดภัยในการใช้ยาของผู้ป่วย

คำสำคัญ: อันตรกิริยาระหว่างยา การใช้ยาหลายชนิด ผู้ป่วยสูงอายุโรคมะเร็ง ยาเคมีบำบัด

Introduction

Thailand has officially achieved the status of a complete aged society (1). This demographic shift is directly associated with a higher prevalence of cancer (2). Elderly cancer patients frequently experience age-related physiological changes, including reduced hepatic and renal functions, altered pharmacokinetics, and multiple comorbidities requiring complex medication regimens (3). Consequently, polypharmacy is highly prevalent in elderly cancer patients and substantially increased the risk of drug-drug interactions (DDIs), especially in oncological settings where patients receive chemotherapy, supportive care medications, and treatments for chronic disease (4,5). Previous studies have reported a substantial burden of potential DDIs among older adults (6). In oncology settings, the risk of DDIs is further increased because anticancer regimens are commonly administered together with supportive care and treatments for multiple comorbidities (7).

Global studies have reported that prevalence rates among elderly cancer patients vary considerably depending on study populations, clinical settings, and screening methodologies. A study from Portugal reported a DDI prevalence of 76.5% among older patients receiving chemotherapy, particularly in patients with polypharmacy (PP) and complex supportive care regimens (8). In contrast, a Jordanian study using the American Geriatrics Society (AGS) Beers Criteria identified potentially inappropriate drug combinations in only 15.6% of elderly cancer patients (9). These findings demonstrate the substantial heterogeneity of DDI prevalence estimates across geriatric oncology studies and underscore the influence of different screening tools and prescribing practices. A systematic review reported a pooled prevalence of 50.7% (10). PP has consistently been identified as one of the strongest factors associated with DDIs in geriatric oncology populations. Furthermore, patients with metastatic stage may be at increased risk because advanced-stage cancer often requires intensive supportive care, symptom

management, and multidrug treatment regimens (11,12).

These findings indicate a substantial prevalence of potential DDIs. This issue is particularly relevant at Srinagarind Hospital, a major tertiary referral center for complex oncology cases in Thailand. Patients at this facility often receive diverse chemotherapy regimens combined with multiple medications from various sources. Therefore, this study aimed to investigate the specific prevalence, severity, and factors associated with DDIs among elderly cancer patients receiving chemotherapy in a university hospital setting. These findings may support the development of pharmacist-led medication review strategies and systematic screening protocols, together with multidisciplinary approaches, to enhance medication safety in geriatric oncology practice.

Methods

Study Design

This retrospective cross-sectional study was conducted at Srinagarind Hospital. Data were extracted from the electronic medical records of elderly cancer patients admitted between January and December 2023. This study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice Guidelines. The protocol was reviewed and approved by the Human Research Ethics Committee of Khon Kaen University (Ref. No. HE671719). The need for informed consent was waived by the Human Research Ethics Committee of Khon Kaen University.

Study Population

The target population included all hospitalized elderly patients, who were defined as individuals aged 65 years and older. This age threshold was selected in accordance with the 2023 AGS Beers Criteria®, which is specifically developed for adults aged ≥ 65 years and is widely used internationally in geriatric pharmacotherapy research and medication safety assessment. The study included elderly patients diagnosed with any

type and stage of cancer who received intravenous chemotherapy. Data were retrospectively retrieved from inpatient electronic medical records. The unit of analysis was the individual patient rather than hospitalization episodes. For patients with multiple admissions during the study period, only one hospitalization record was included in the analysis. Medication exposure was defined as all drugs administered during the index hospitalization only, including chemotherapy, supportive medications, and drugs for comorbidities.

Patients were eligible for inclusion if they were aged 65 years or older with a confirmed diagnosis of cancer and had been admitted as inpatients. Eligible participants must have received at least one dose of intravenous chemotherapy during the index hospitalization. Completion of the full chemotherapy course was not required. In addition, patients were required to have received at least two concomitant medications (e.g., antiemetics, analgesics, or medications for comorbidities), as documented in the inpatient electronic medical record during the index hospitalization. Patients were excluded if their complete inpatient medication list, including drug names and dosages, could not be verified from the electronic medical record. In addition, patients who refused treatment or were discharged against medical advice before receiving the planned medication regimen were not included in the study.

Sample size was estimated using the Taro Yamane formula based on the total number of elderly cancer patients admitted to the chemotherapy unit during the study period, yielding a minimum required sample size of 384 patients. Eligible patients were identified from inpatient chemotherapy records between January and December 2023, and simple random sampling was performed using Microsoft Excel-generated random numbers. Each patient was included only once during the study period. The final sample comprised 390 patients.

Sample size estimation was also based on the events-per-variable (EPV) principle for multivariable logistic regression. With six independent variables planned for inclusion in the model and a recommended minimum of 10 events per variable, at least 60 patients experiencing the outcome (i.e., at least one potential DDI) were required. A systematic review reported a pooled prevalence of 50.7% for DDIs in this population (10). A minimum sample size of approximately 120 patients was required. However, the final sample comprised 390 patients, which exceeded the minimum EPV requirement and was considered adequate for the multivariable analysis.

Data Collection and Instruments

Demographic data variables included age and sex. Clinical characteristics included cancer type, cancer stage, renal function, number of comorbidities, and underlying diseases. Medication profiles included all medications prescribed during the index hospitalization, including chemotherapy agent, supportive care medications, palliative medications, and treatments for comorbidities. The study collected information on drug name, dosage regimen, route of administration, and frequency of administration. DDIs were identified and evaluated using two standardized tools. The first tool was Lexicomp® database which was used to determine potential DDIs and classify their severity according to the Risk Rating system (A, B, C, D, and X) (13). The second tool was the 2023 AGS Beers Criteria®, which evaluates DDIs based on pharmacological mechanisms. It specifically identifies medications that are considered potentially inappropriate medications (PIMs) in elderly, on the basis of evidence of the risk of harm in this geriatric population (14). Therefore, the findings from each tool are reported separately throughout this study, and the two prevalence figures are not directly comparable.

Classification of DDIs

DDIs were classified according to pharmacokinetic or pharmacodynamic mechanisms,

and were also categorized according to their associated risk level. This classification helps determine the urgency and response.

The Lexicomp® drug-interaction database was used to classify potential DDIs according to a five-category risk classification system (13). The categories and their corresponding definitions are as follows: category A (no known interaction) indicates no evidence of a pharmacodynamic or pharmacokinetic interaction; category B (no action needed) denotes the presence of a potential interaction for which clinical data supporting its significance are limited or absent; category C (monitor therapy) includes interactions for which evidence suggests that clinically significant consequences may occur; category D (consider therapy modification) comprises interactions for which evidence indicates clinical significance and for which specific measures are recommended to minimize the risk of toxicity; and category X (avoid combination) represents interactions in which concomitant use of the two drugs is contraindicated.

The severity of potential drug–drug interactions was classified into three levels. Minor interactions were defined as those with limited clinical consequences that required only minimal monitoring. Moderate interactions referred to interactions capable of exacerbating the patient's clinical condition and therefore necessitating either close monitoring or therapeutic adjustment. Major interactions were defined as those with potentially life-threatening consequences that required immediate clinical intervention or avoidance of the combination.

Statistical Analysis

The data were analyzed using the Statistical Package for Social Sciences (SPSS), version 27.0. Descriptive statistics were used to summarize patient characteristics. Continuous variables were presented as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR), depending on data distribution, while categorical variables were expressed as frequencies and percentages.

Variables with $P < 0.20$ in univariable analysis were subsequently included in the multivariable model. Univariable logistic regression analysis was initially performed to identify factors associated with potential DDIs. Variables with a $P < 0.20$ were entered into the multivariable logistic regression model. Although age met the screening criterion ($P < 0.20$), it was excluded to minimize multicollinearity with medication burden. Prior to multivariable analysis, multicollinearity among the remaining independent variables was assessed using variance inflation factor (VIF), with VIF values < 5 considered acceptable (all VIF values < 5). Model goodness-of-fit was evaluated using the Hosmer-Lemeshow test. The test indicated good model fit ($P > 0.05$). Continuous variables were assessed for linearity with the log-odds using the Box-Tidwell procedure. Missing data were handled using complete-case analysis. Results from the univariable logistic regression are reported as unadjusted odds ratios (ORs), whereas those from the multivariable analysis are presented as adjusted odds ratios (aORs) with 95% confidence intervals (CIs). Statistical significance was defined as a $P < 0.05$.

Results and Discussion

Patient characteristics

The study included 390 elderly cancer patients with a median age of 69 years (IQR, 67–73), of whom 58.0% were male (Table 1). These demographic characteristics are consistent with previous studies, which reported a male predominance (55.6–69.1%) and a similar median age range of 68–71 years (15–16). Colorectal cancer was the most common cancer (40.0%), followed by cholangiocarcinoma (12.6%), aligning with regional epidemiological data (16,17). Regarding comorbidities, 64.4% of patients had at least one underlying disease, with hypertension being the most common (41.0%). Although its prevalence is slightly lower than previously reported rates of 42.8%–62.0% seen in general elderly populations, hypertension

Table 1. Characteristics of cancer patients (n=390)

Patient Characteristics	n (%)
gender (n, %)	
male	226 (58.0)
female	164 (42.0)
age [median (IQR)]	69 (67–73)
cancer type (number, %)	
colorectal	156 (40.0)
cholangiocarcinoma	49 (12.6)
hepatocellular carcinoma	28 (7.2)
pancreatic cancer	25 (6.4)
hematologic malignancy	22 (5.6)
lung	21 (5.4)
bladder	20 (5.1)
head and neck	19 (4.9)
gynecologic malignancy	18 (4.6)
stomach	16 (4.1)
other cancers	16 (4.1)
cancer stage (n, %)	
non-metastatic	218 (55.9)
metastatic	172 (44.1)
no. of comorbidities [median (IQR)]	1 (0–2)
presence of comorbidities ¹ (n, %)	251 (64.4)
hypertension	160 (41.0)
diabetes mellitus	105 (26.9)
dyslipidemia	51 (13.1)
benign prostatic hyperplasia	25 (6.4)
others	49 (12.6)
renal function (n, %)	
CKD stage 1	121 (31.0)
CKD stage 2	183 (46.9)
CKD stage 3a	54 (13.8)
CKD stage 3b	10 (2.6)
CKD stage 4	12 (3.1)
CKD stage 5	10 (2.6)
number of medications (n, %)	
<5 medications	35 (9.0)
5–9 medications	255 (65.4)
≥10 medications	100 (25.6)

1: Patients may have more than one comorbidity.

is a key comorbidity that complicates medication regimens in elderly cancer patients (11, 15–16). Approximately 44.1% of patients were in the metastatic stage. A significant proportion (65.4%) were exposed to polypharmacy (≥ 5 medications), highlighting the complexity of oncological care which often requires multiple supportive and therapeutic agents (4) (Table 1).

Prevalence of potential DDIs

The prevalence of potential DDIs identified using the Lexicomp® database was 97.4%, whereas potentially inappropriate drug combinations identified using the 2023 AGS Beers Criteria® accounted for 23.8% (Table 2). A total of 3,101 DDI occurrences involving 474 unique interacting drug pairs were identified. The substantial difference in prevalence between the two screening tools likely reflects their distinct clinical purposes. The Lexicomp® database provides broad interaction screening and captures a wide range of pharmacokinetic and pharmacodynamic interactions commonly encountered in oncology practice. In contrast, the 2023 AGS Beers Criteria® focuses specifically on clinically important and potentially inappropriate drug combinations in older adults. These findings suggest that the two tools provide complementary perspectives for medication safety assessment in geriatric oncology patients.

Classification of potential DDIs

To improve the clinical interpretability of database-identified DDIs, interactions were categorized according to therapeutic intent and clinical context. These categories included intended pharmacological combinations routinely used in oncology protocols, intended combinations requiring protocol-based monitoring, and potentially clinically significant DDIs requiring intervention or enhanced surveillance. The Lexicomp® database identified a total of 474 DDI pairs, categorized into those arising from chemotherapy regimens and supportive symptom management as

Table 2. Prevalence of potential DDIs according to Lexicomp® and 2023 AGS Beers Criteria®

Characteristics	Lexicomp®	2023 AGS Beers Criteria®
total number of patients	390	390
patients with ≥ 1 DDI, n (%)	380 (97.4%)	93 (23.8%)
total number of DDI pairs	3101	146
median number of DDI pairs per patient (IQR)	5 (4–7)	0 (0–1)

Note: A total of 3,101 DDI occurrences involving 474 unique interacting drug pairs were identified.

shown in Table 3. Several commonly observed DDIs represented intended pharmacological combinations routinely used in standard oncology protocols (Table 3). Frequently encountered combinations included folinic acid with 5-FU and oxaliplatin with 5-FU, reflecting

standard components of FOLFOX- and FOLFIRI-based chemotherapy regimens. Carboplatin with paclitaxel and oxaliplatin with docetaxel represent established regimen combinations used in gynecologic and gastrointestinal cancers.

Table 3. Classification of database-identified DDIs according to clinical context (total DDI occurrences = 3,101)

A. Intended pharmacological combinations routinely used in standard oncology regimens

Drug pairs	Frequency (%)	Lexicomp® risk rating	Chemotherapy regimen	Clinical interpretation
folinic acid + 5-FU	242 (7.8)	C	FOLFOX/FOLFIRI	intended synergistic enhancement of 5-FU activity
oxaliplatin + 5-FU	173 (5.6)	B	FOLFOX	standard chemotherapy combination
carboplatin + paclitaxel	17 (0.6)	D	PT (Gynecologic/ lung cancers)	standard regimen requiring sequence-dependent administration
cisplatin + etoposide	4 (0.1)	C	EP (Small cell lung cancer)	standard chemotherapy combination
doxorubicin + cyclophosphamide	3 (0.1)	C	AC	routine breast cancer chemotherapy protocol
nivolumab + ipilimumab	2 (0.1)	B	(Immunotherapy combination)	standard immunotherapy combination
oxaliplatin + docetaxel	2 (0.1)	D	FLOT (Gastric cancer) (19)	requires close toxicity monitoring due to overlapping toxicities

Note: Percentages were calculated based on the total number of DDI occurrences identified by the Lexicomp® database (n=3,101), not on the number of patients.

Table 3. Classification of database-identified DDIs according to clinical context (total occurrences drug pairs=3101) (continued)

B. Potentially clinically significant DDIs requiring monitoring or intervention (total DDI occurrences = 3,101)

Drug pairs	Frequency (%)	Lexicomp® risk rating	Potential clinical concern
metoclopramide + 5-FU	199 (6.4)	B	increased extrapyramidal/CNS adverse effects.
lorazepam + metoclopramide	180 (5.8)	C	metoclopramide may increase CNS depressant effects of CNS depressants.
5FU + folic acid	80 (2.6)	C	folic acid may increase adverse/toxic effects of fluorouracil products
lorazepam + olanzapine	75 (2.4)	C	CNS depressant effects may increase with coadministration.
metformin + ondansetron	42 (1.4)	C	ondansetron may increase serum concentrations of metformin.
lorazepam + morphine	36 (1.2)	D	CNS depressants may increase CNS depressant effects of Opioid agonists.
glipizide + tramadol	25 (0.8)	C	increase hypoglycemic effects of hypoglycemia-associated agents.
5-FU + olanzapine	22 (0.7)	C	QT prolongation/CNS adverse effects.
warfarin + 5FU	9 (0.3)	D	monitor INR and signs/symptoms of bleeding.
paclitaxel + olanzapine	5 (0.2)	C	monitor blood pressure closely, and caution patients regarding the potential for orthostatic hypotension and syncope.

Note: Percentages were calculated based on the total number of DDI occurrences identified by the Lexicomp® database (n=3,101), not on the number of patients.

Although some of these combinations were categorized as Risk C or Risk D interactions by the Lexicomp® database, many represented intentional protocol-based regimens in which the therapeutic benefits outweighed the interaction risks when appropriate monitoring was implemented. Therefore, the high prevalence of DDIs identified in this study should not be interpreted as universally inappropriate prescribing.

CNS-related DDIs involving opioids, benzodiazepines, gabapentinoids, and sedating antiemetics may increase the risk of excessive sedation, respiratory depression, falls, and delirium in older

adults. Pharmacists should therefore closely monitor sedation status, medication duplication, and cumulative CNS burden, particularly in frail patients receiving multiple supportive care medications.

Regarding chemotherapy-related interactions, the combination of oxaliplatin and 5-FU was the most frequent (5.6%, Risk B). Although classified as low risk, specific combinations such as carboplatin and paclitaxel (0.6%) and oxaliplatin and docetaxel (0.1%) reached Risk D, necessitating therapy modification. In the context of supportive care, the interaction between folic acid and 5-FU (7.8%, Risk C) and folic acid and 5-FU (2.6%, Risk C) were highly prevalent. These

Table 4. Potential inappropriate drug combinations according to the 2023 AGS Beers Criteria® (n=93)

Potential inappropriate drug combinations	n (%) ^a
opioid with benzodiazepines	72 (77.4)
concurrent use of ≥ 3 CNS-active drugs	47 (50.5)
opioid with gabapentin	17 (18.3)
concurrent use of anticholinergic agents	9 (9.6)
RAS inhibitor with potassium-sparing diuretic	1 (1.1)

^a Percentages were calculated based on the number of patients with at least one DDIs identified by the 2023 AGS Beers Criteria® (n=93); Patients may have more than one potentially inappropriate drug combination.

combinations are often therapeutically intended to enhance the cytotoxic efficacy of 5-FU (5,13), they require vigilant monitoring for exacerbated hematological and gastrointestinal toxicities (15). It is noteworthy that not all identified DDIs represent clinical hazards. The combination of folinic acid (leucovorin) with 5-FU represents an intentional pharmacological synergism that forms the cornerstone of FOLFOX and FOLFIRI regimens. In this context, the interaction enhances the cytotoxic effect of 5-FU by stabilizing the ternary complex with thymidylate synthase.

The high prevalence of DDIs (97.4%) observed in this study surpasses those reported in similar geriatric oncology cohorts in Portugal (76.5%) and Saudi Arabia (79.4%) (8,17), likely due to the comprehensive sensitivity of the Lexicomp® database in capturing interactions between intensive chemotherapy and supportive care agents. Consistent with previous oncology research, these results underscore that most interactions are of moderate severity and do not necessarily require cessation of therapy but demand pharmacist-led monitoring to ensure safety without compromising oncological outcomes (18).

Potentially inappropriate drug combinations

When evaluated using the 2023 AGS Beers Criteria®, the most common potentially inappropriate

drug combinations involved opioids with benzodiazepines (77.4%), concurrent use of three or more CNS-active drugs (50.5%), and opioids with gabapentin (18.3%) (Table 4). These combinations are recognized as high-risk prescribing patterns in older adults because they may increase the risk of excessive sedation, respiratory depression, impaired cognition, and falls (14). The predominance of CNS-related interactions in this study likely reflects the extensive use of opioid analgesics, antiemetics, anxiolytics, and supportive care medications in elderly cancer patients. These findings highlight the importance of careful evaluation of cumulative CNS depressant burden during medication review in geriatric oncology practice.

Risk category

Among the 474 unique interacting drug pairs identified by Lexicomp® database, Risk C interactions were the most common (268 pairs, 56.5%), followed by Risk B interactions (111 pairs, 23.4%). Risk D interactions accounted for 14.8% (70 pairs), while Risk X interactions represented 4.0% (19 pairs), and Risk A interactions accounted for 1.3% (6 pairs) as shown in Figure 1. These findings indicate that most identified interactions required clinical monitoring rather than immediate discontinuation of therapy. Nevertheless, Risk D and Risk X interactions remain clinically important in elderly cancer patients because age-related physiological decline, multimorbidity, and reduced organ reserve may increase susceptibility to adverse drug events. Pharmacist-led medication review and individualized risk assessment may therefore help optimize medication safety in this population.

Factors associated with DDIs

Table 5 displays the results on univariable and multivariable logistic regression analysis of factors associated with potential DDIs by Lexicomp® database and potentially inappropriate drug combinations by AGS Beers Criteria®. Polypharmacy was independently

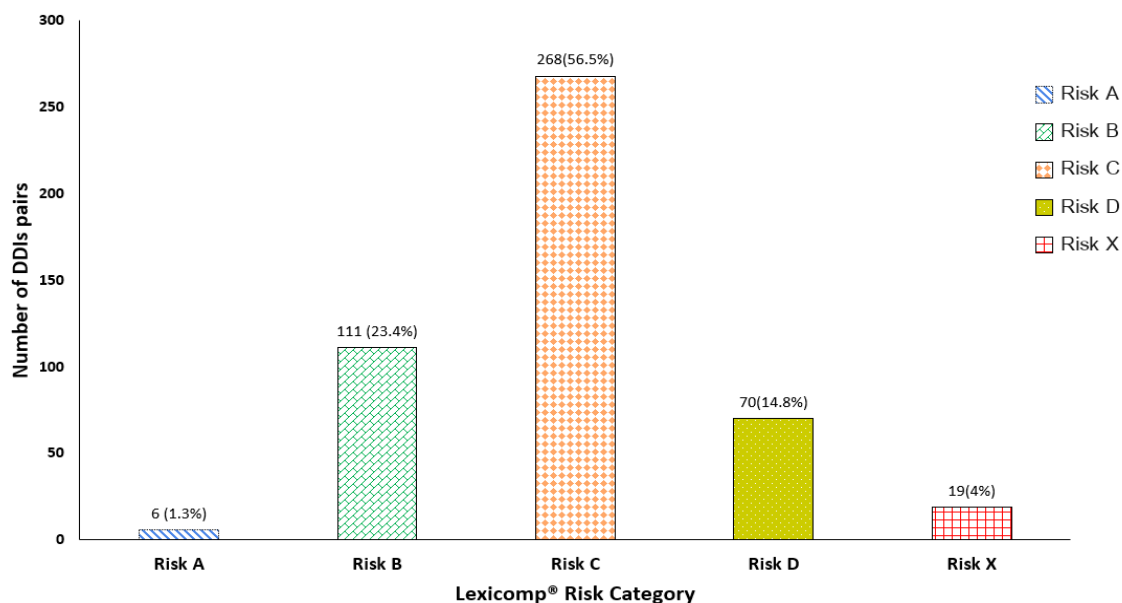


Figure 1. Distribution of unique interacting drug pairs according to Lexicomp® risk classification

associated with DDIs in both screening approaches. Patients receiving ≥ 10 medications had markedly increased odds of potential DDIs according to the Lexicomp® database (aOR 18.04; 95% CI: 6.05–53.86; $P < 0.001$) and potentially inappropriate drug combinations according to the 2023 AGS Beers Criteria® (aOR 9.64; 95% CI: 1.21–76.71; $P = 0.032$). This strong association is clinically plausible because greater medication burden increases opportunities for pharmacokinetic and pharmacodynamic interactions, consistent with previous findings in geriatric oncology populations (11,12). Gynecologic malignancy was also independently associated with Lexicomp®-identified potential DDIs, possibly reflecting the complexity of treatment regimens that often include platinum-based chemotherapy, antiemetics, corticosteroids, analgesics, and medications for treatment-related adverse effects. Even when such combinations are therapeutically intended, monitoring remains necessary because toxicity may be amplified in older patients with multimorbidity and reduced physiological reserve.

Metastatic status showed different findings across the two tools. It was significantly associated with Lexicomp®-identified potential DDIs (aOR 1.88; 95% CI: 1.18–3.00; $P = 0.008$), but was not retained in the AGS

Beers Criteria® multivariable model because it did not reach statistical significance in univariable analysis ($P = 0.052$). This discrepancy may be explained by the distinct purposes of the tools. The Lexicomp® database captures a broad range of pharmacokinetic and pharmacodynamic interactions and may be more sensitive to medication complexity in advanced cancer, whereas the AGS Beers Criteria® focuses specifically on age-related potentially inappropriate drug combinations. Patients with metastatic disease often require intensive supportive care and symptom-control medications, which may further increase the likelihood of potential DDIs.

These findings support systematic multidisciplinary, pharmacist-led medication review in geriatric oncology care, particularly among patients with excessive polypharmacy, metastatic disease, and complex supportive-care regimens. However, several estimates had relatively wide confidence intervals, indicating limited precision of estimated effects. Therefore, the magnitude of these associations should be interpreted cautiously.

Limitations

This study has several limitations. First, its retrospective cross-sectional design does not allow

Table 5. Univariable and multivariable logistic regression analysis of factors associated with potential DDIs by Lexicomp® database and potentially inappropriate drug combinations by AGS Beers Criteria® (n=390)

Variables	Univariable logistic regression				Multivariable logistic regression			
	by Lexicomp®		by Beers Criteria®		by Lexicomp®		by AGS Beers Criteria®	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
gender								
female	1.06 (0.71–1.60)	0.774	0.91 (0.48–1.72)	0.760				
age	1.03 (0.98–1.08)	0.261	1.05 (0.98–1.13)	0.180				
number of comorbidities	1.10 (0.91–1.32)	0.317	0.94 (0.69–1.27)	0.670				
number of medications								
5–9 medications	3.50 (1.32–9.31)	0.012*	3.47 (0.45–26.51)	0.230	4.14 (1.48–11.58)	0.007*	3.87 (0.50–30.03)	0.200
≥10 medications	13.60 (4.83–38.31)	<0.001*	8.31 (1.07–64.55)	0.040*	18.04 (6.05–53.86)	<0.001*	9.64 (1.21–76.71)	0.032*
metastatic status								
metastatic (M1)	1.55 (1.03–2.32)	0.035*	1.89 (0.99–3.59)	0.052	1.88 (1.18–3.00)	0.008*	N/A	N/A
cancer type								
head and neck	1.92 (0.97–3.80)	0.061*	1.62 (0.62–4.21)	0.320	1.84 (0.87–3.88)	0.111	1.042 (0.53–3.77)	0.480
gynecologic malignancy	2.53 (1.26–5.11)	0.009*	0.49 (0.11–2.17)	0.350	3.59 (1.65–7.80)	0.001*	0.50 (0.11–2.21)	0.360
hematological malignancy	1.06 (0.43–2.65)	0.898	0.43 (0.05–3.34)	0.420	1.11 (0.40–3.04)	0.843	0.36 (0.05–2.80)	0.330
other cancers	3.46 (1.43–8.36)	0.006*	2.88 (1.06–7.86)	0.040*	5.26 (1.96–14.16)	0.001*	3.32 (1.17–9.40)	0.024*

*P<0.05 indicates statistical significance; N/A: Not entered into the multivariable model

Note: Variables not entered into multivariable model are left blank.

causal relationships between associated factors and DDIs to be established. Second, the study was conducted in a single university hospital that serves as a tertiary oncology referral center. Therefore, prescribing patterns and patient complexity in the study may differ from those in other healthcare settings, limiting generalizability. Third, DDIs were identified using screening databases rather than confirmed clinical adverse events. Consequently, some detected interactions may not have resulted in clinically significant harm. In particular, several identified DDIs reflected intended pharmacological combinations routinely used in standard chemotherapy protocols, which may have contributed to overestimation of clinically harmful interactions. Conversely, over-the-counter medications, herbal products, and medications obtained outside the hospital were not captured in the electronic medical records, potentially leading to underestimation of some DDIs. Fourth, the association between polypharmacy and DDIs may partly reflect underlying disease severity and treatment complexity. Residual confounding from unmeasured clinical and medication-related factors may remain despite multivariable adjustment. In addition, because the prevalence of potential DDIs was very high, the relatively small number of non-event observations may have reduced the precision and stability of some regression estimates. Future prospective studies evaluating clinically significant adverse outcomes related to DDIs in geriatric oncology patients are warranted.

Conclusion

This study demonstrated a high prevalence of potential DDIs among elderly cancer patients receiving chemotherapy in a university hospital setting, particularly among patients with polypharmacy and metastatic disease. Excessive polypharmacy was strongly associated with the occurrence of DDIs, highlighting the impact of complex medication regimens

in geriatric oncology practice. Most identified interactions were classified as moderate severity and included both clinically significant DDIs and intended pharmacological combinations routinely used in standard oncology protocols. The prevalence estimates differed substantially between the Lexicomp® database and the 2023 AGS Beers Criteria®, reflecting the complementary roles of comprehensive interaction databases and geriatric-specific screening tools in evaluating medication safety. Pharmacist-led medication review, in conjunction with multidisciplinary collaboration and careful clinical interpretation of database-identified DDIs, may help improve medication safety in elderly cancer patients. However, because the identified DDIs were based on database screening, adverse clinical outcomes were not confirmed. Therefore, further prospective studies are warranted to evaluate the actual clinical consequences and patient outcomes associated with DDIs in geriatric oncology populations.

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Use of Artificial Intelligence in Article Writing

The authors acknowledge that Gemini-3.1-pro-preview was utilized specifically for language refinement, grammatical correction, and polishing the prose to ensure clarity and professional academic tone. It was also used to assist in the initial drafting of certain sections, specifically the translation and structural organization of the Results and Discussion sections.

The authors confirm that they have thoroughly reviewed and verified the accuracy of all content generated or modified by the AI. The authors assume full responsibility for the integrity, originality, and reliability of the final manuscript, ensuring it adheres to all academic and ethical standards of the Thai Journal of Pharmacy Practice.

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