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Inappropriate Medication Use in Elderly Surgical Patients: A National Study

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Abstract

Objectives—To determine the prevalence and factors associated with use of potentially inappropriate medications (PIMs) in elderly surgical patients.

Design—Retrospective cohort study.

Setting—379 acute care hospitals participating in the nationally representative Perspective database (2006-2008).

Participants—Individuals age 65 and older undergoing major inpatient gastrointestinal, gynecologic, urologic, and orthopedic surgery (n=272,351).

Measurements—Medications were classified as PIMs using previously published criteria. Information about patient and provider characteristics and administration of PIMs was obtained from hospital discharge file data. We used logistic regression techniques to examine factors associated with use of PIMs in the perioperative period.

Results—272,351 patients aged 65 or older underwent one of our target surgical procedures, and one quarter of patients received at least one PIM during their surgical admission. Meperidine was the most frequently prescribed PIM (37,855, 14% of patients). In adjusted analysis, PIM use was less likely as age advanced (adjusted OR 0.98 per year of age, 95%CI 0.97-0.98) and among men (adjusted OR 0.83, 95%CI 0.81-0.85). PIMs were most likely to be prescribed to patients cared for by an orthopedic surgeon (adjusted OR 1.22, 95%CI 1.08-1.40 v. general surgeons). Compared to patients undergoing surgery in the Northeast, patients in the West and South were more likely to receive a PIM (adjusted OR 1.79, 95%CI 1.02-3.16 and adjusted OR 2.24, 95%CI 1.38-3.64, respectively).

Conclusions—Receipt of PIMs in elderly surgical patients is common and varies widely across providers, geographic regions, and by patient characteristics. Interventions aimed at reducing the use of PIMs in the perioperative period should be considered in quality improvement efforts.

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Keywords

surgery; potentially inappropriate medications (PIMs); older adults

As the population ages, an increasing number of elderly patients will be candidates for major surgery. Currently, over 50% of orthopedic, urologic, and general surgery procedures are performed in patients age 65 and older.¹ Numerous studies have documented that morbidity and mortality after major surgery increases dramatically with age.²⁻⁴ For this reason, there is increasing interest in identifying potential processes of care that can improve surgical care in the growing population of elderly patients.^{5, 6}

Although there is great enthusiasm for improving surgical care in the elderly, there is little agreement about where to start. A recent review of potential quality indicators for elderly surgical patients identified over ninety candidate measures.⁵ One potential quality indicator – the avoidance of high risk medications – is easily measured and an attractive target for quality improvement. An explicit list of potentially inappropriate medications (PIMs) in the elderly was initially proposed by Beers et al (ref) and subsequently refined by Zhan et al.⁷ Zhan criteria medications include 33 agents considered inappropriate for use in individuals age 65 and older. PIM use has been associated with adverse drug reactions in elders such as delirium, falls, and urinary retention.⁸ This list contains several types of medications – including sedatives and pain medications – that are commonly used in surgical patients. Although PIM use has been studied in elder patients hospitalized with medical diagnoses,⁸⁻¹¹ it has not been studied in the elder surgical population.

Currently, the prevalence and risk factors for perioperative PIM use in elder surgical patients is unknown. For this reason, we used data from a nationally representative sample of US hospitals (Perspective database) to study PIM use among patients age 65 and older undergoing major gastrointestinal, urologic, gynecologic, and orthopedic surgery. To better understand risk factors for receipt of a PIM in the perioperative period, we examined patient and provider characteristics associated the PIM use.

Methods

Database and subjects

We used the 2006-2008 Perspective database (Premier Inc., Charlotte, North Carolina) to identify a retrospective cohort of surgical patients age 65 and older. The Perspective database was developed by Premier Healthcare Informatics for measuring quality and health care utilization. Premier hospitals are located in all regions of the United States, are predominantly small to mid-size non-teaching facilities, and serve a largely urban patient population. Using ICD-9-CM procedure codes defined by the Healthcare Cost and Utilization Project Clinical Classification System, we identified patients age 65 and older undergoing major inpatient gastrointestinal, urologic, gynecologic, and orthopedic surgery. (<http://www.hcupus.ahrq.gov/toolssoftware/ccs/ccs.jsp>). The Healthcare Cost and Utilization Project Clinical Classification System is a tool for clustering ICD-9-CM procedure codes into clinically meaningful categories. To capture patients undergoing elective inpatient surgery, we excluded patients admitted through the emergency department, transferred from an acute care hospital or had a length of stay shorter than 3 days. Our final cohort included 272,351 who underwent elective inpatient surgery.

Patient and provider characteristics

Patient demographic data were obtained from the hospital discharge file data. We used ICD 9 diagnosis codes to assess patient comorbidities using methods described by Elixhauser et

al.¹² Comorbidities with prevalence greater than 1% were included in the analysis. Hospital characteristic including teaching status, location type (rural v. urban), and geographic region were obtained from the Premier database. Information about the specialty of the attending physician and inpatient consultation by a non-surgeon (internist, hospitalist, family practitioner, or geriatrician) was obtained from discharge abstracts.

Definition of PIM use

Perspective contains a date-stamped log of all medications charged for during each hospitalization. A charge for a medication any time between the day of surgery and the day of discharge was considered postoperative receipt of a drug. We defined potentially inappropriate medication use as receipt of one or more of the 33 drugs classified as potentially inappropriate in individuals age 65 and older as defined by Zhan et al.⁷ In a review by expert panel, PIMs were classified in 3 categories – ‘always avoid’, ‘rarely appropriate’, and ‘some indications but often misused’. Because administrative data are limited in their ability to capture all clinical conditions, we were not able to determine the specific indication for each medication administered. For this reason, we did not include medications classified as having ‘some indications’ in the elderly in our definition of PIM exposure used in our risk factor analysis. Summary statistics of patient and provider variables presented as proportions for categorical variables and means and standard deviations for continuous variables. Frequency of PIM use was also measured at the individual hospital level among hospitals with at least 50 surgical patients during the study period.

Statistical analysis

We first described study patients and providers using univariable methods. Multivariable GEE models (Proc Genmod in SAS) were used to adjust for clustering of patients within hospitals and calculate adjusted odds ratios and 95% confidence intervals for receipt of PIMs. Models were constructed using manual variable selection methods. Covariates (confounding factors) were selected for inclusion if they were associated with the outcome at $p < 0.01$. All analyses were carried out using SAS version 9.2 (SAS Institute, Inc. Cary, NC). The institutional review board at UCSF approved our study.

Results

Patient and provider characteristics (Table 1)

272,351 patients age 65 and older underwent one of the nine procedures examined. The most frequently performed procedures were arthroplasty ($n=139,958$), hip replacement ($n=67,401$) and colorectal resection ($n=40,400$). The mean age was 75 and 35% were male. Seventy five percent were white. The most common comorbidities were hypertension (70%), diabetes (21%), and iron deficiency anemia (19%).

The majority of patients (71%) were under the care of an orthopedic surgeon during their surgical hospitalization. General surgeons were the attending physicians for over 40,000 patients. Overall, 26% of surgical patients received a medical consultation after surgery. Hospitals were most frequently located in the southern United States (43%) and were in an urban setting (88%).

Frequency of PIM use (Table 2)

Overall, over half of patients undergoing surgery received a PIM during their surgical hospitalization. Twenty five percent received a PIM categorized as ‘always avoid’ or ‘rarely appropriate’. Among patients receiving an ‘always avoid’ medication, meperidine was the most frequently prescribed medication with 37,855 (14%) patients receiving the drug after

surgery. In the ‘rarely appropriate’ category, the most commonly prescribed medications were sedatives and muscle relaxants – diazepam (3%) and cyclobenzaprine (3%). Two medications commonly used in surgical patients – diphenhydramine and promethazine – were given to a large number of patients (59,967 (22%) and 52,027 (19%), respectively). There was substantial variation in frequency of ‘always avoid’ or ‘rarely appropriate’ PIM use across individual hospitals (Figure 1). Over 40% of all hospitals administered a PIM to fewer than 20% of elderly patients. Very high frequency PIM use (>80%) was observed in only 4 hospitals. Variation in meperidine use at the hospital level was pronounced. In over a quarter (26%) of all hospitals, fewer than 5% of patients received meperidine during their surgical hospitalization. In nearly half of all hospitals (47%), fewer than 10% of patients received meperidine.

Patient and provider characteristic associated with PIM use (Table 3)

In multivariate analysis, several patient factors were associated with receipt of a “always avoid” or “rarely appropriate” PIM. Men were less likely to receive a PIM than women (adjusted odds ratio (AOR) 0.83, 95%CI 0.81-0.85). Compared to younger patients (age 65-69), patient in all older age groups were less likely to receive a PIM – 30% v. 26% for age 70-74 (AOR 0.89, 95%CI 0.87-0.91), 24% for age 75-79 (AOR 0.82, 95%CI 0.79-0.85), 22% for age 80+ (AOR 0.71, 95%CI 0.68-0.74). Both black and Hispanic elders were less likely to receive a PIM than white elders (AOR 0.80, 95%CI 0.76-0.85 and AOR 0.88, 95%CI 0.81-0.96, respectively). Several individual patient comorbidities were associated with small increases in the risk of receiving a PIM. Patients diagnosed with COPD (AOR 1.09, 95%CI 1.07-1.12), congestive heart failure (AOR 1.06, 95%CI 1.02-1.10), hypothyroidism (AOR 1.05, 95%CI 1.03-1.07), depression (AOR 1.10, 95%CI 1.07-1.14), psychoses (AOR 1.17, 1.09-1.1.25), anemia (AOR 1.04, 95%CI 1.01-1.07), weight loss (AOR 1.24, 95%CI 1.15-1.34), and rheumatoid/collagen disorders (AOR 1.08, 95%CI 1.03-1.14) were more likely to receive a PIM than patients who were not diagnosed with these conditions. Compared to patients without diabetes, diabetics were less likely to receive a PIM (AOR 0.94, 95%CI 0.92-0.96).

There was substantial variation in PIM use across physician and hospital type. PIM was common among patients under the care of orthopedic surgeons (26%) 22% general surgeons (22%), gynecologic surgeons (23%) and urologic surgeons (19%). Compared with general surgery specialty, orthopedic surgery specialty was the single surgical specialty significantly associated with PIM administration after adjustment for other patient and provider characteristics (AOR 1.22, 95%CI 1.08-1.40). Rates of PIM use were highest among patients under the care of non-surgeon physician (32%, AOR 1.40, 95%CI 1.26-1.55). The presence of a medical consultation was associated with increased likelihood of receiving a PIM (AOR 1.09, 95%CI 1.04-1.14). Among all hospital characteristics examined, only geographic region was independently associated with increased use of PIM in the elderly. Rates of PIM use varied across regions -- 14% in the Northeast, 23% in the Midwest, 26% in the West, and 30% in the South. Compared to hospitals in the Northeast, hospitals in the West and South and were more likely to prescribe a PIM during the postoperative period (AOR 1.79, 95%CI 1.02-3.16 and AOR 2.24, 95%CI 1.38-3.64, respectively).

Discussion

In this retrospective cohort of elderly patients undergoing elective major surgery, we found a very high prevalence of PIM use. In addition, we found substantial variation across patients and providers. Potentially inappropriate medication was associated with younger age, female gender, white race, and several individual comorbid conditions. Two provider characteristics – orthopedic specialty and medicine consultation – were associated with increased PIM

prescribing. Elderly patients who underwent surgery in the South were more likely to receive a PIM compared to patients who underwent surgery in other geographic regions.

Although our study examines PIM use among surgical patients, our findings are consistent with prior studies of older adults hospitalized with medical diagnoses.⁷⁻¹⁰ Zhan et al found that over 20% of community-dwelling elderly patients in a nationally representative survey had received at least one PIM.⁷ In a retrospective study of elders hospitalized with medical diagnoses, Rothberg et al found that nearly half of the patients received a PIM during their hospital stay.⁹ Similar to our findings, they found that men and patients age 85 and older were less likely to receive a PIM. They also found that the proportion patients receiving PIMs varied regionally and was highest in the Southern United States. Studies of PIM use in community dwelling elders have also found regional variation in prescribing patterns.^{9, 13} Variation in PIM use by physician specialty has also been documented among patients admitted with medical diagnoses where cardiologists and internists are more likely to prescribe PIMS than geriatricians.⁹ Smaller studies examining meperidine use in hospitalized patients age 65 and older found that surgical patients were 7 times as likely than medical patients to receive meperidine.¹⁴

Our study has several limitations. First, some PIMs prescribed in the inpatient setting may in fact be medications used chronically and their use may not be wholly attributable to the surgical hospitalization. Because the Perspective database does not contain information about outpatient care, we were unable determine if the prescribed PIMs were medications that patients were receiving prior to surgery or if they were medications initiated for the first time in the postoperative period. The most frequently prescribed PIMs, however, were medications often prescribed for postoperative treatment for pain, insomnia, and nausea and are unlikely to reflect continuation of outpatient medication regimens. Second, lists of medications considered inappropriate in the elderly were developed and studied in community dwelling elder and nursing home residents. While the Zhan criteria were developed with outpatients in mind, the drug use recommendations apply strongly to inpatient care. For example, a robust literature shows that meperidine has higher rates of adverse effects than other opioids¹⁵⁻¹⁷, its use is discouraged by the health policy organizations.^{18, 19} Consequently it receives the most stringent warning of “never appropriate” under the Zhan criteria. Other Zhan criteria drugs, also appropriate in selected settings, are very often misused in the hospital environment. For example, benzodiazepines, sedating antihistamines, and strongly anticholinergic tricyclic antidepressants, which are commonly used to help hospitalized patients sleep, are well-recognized risk factors for delirium and a host of other serious outcomes in surgical patients and should only be used rarely and with great caution in hospitalized elders.²⁰ Finally, adverse drug reactions (i.e. delirium, falls) are the most common complications of to capture these complications,²¹ we are unable to measure direct harm from PIM use in this study.

Our study has important implications and suggests opportunities for quality improvement in surgical care in the elderly. Efforts to identify targets for quality improvement in geriatric perioperative care are essential to optimize outcomes in this vulnerable population. Although we found variation across patients and providers, PIM use was frequent in all subgroups of patients and provider types suggesting the need for broad reaching efforts to minimize use of potentially harmful medications in the perioperative period. For medications most frequently prescribed in elder surgical patients – meperidine, diphenhydramine, and promethazine – there are effective and safer alternative analgesics, sedatives, and anti-emetics available. Moreover, hospital-specific rates of meperidine use – the most frequently prescribed ‘always avoid’ PIM – are low in the majority of hospitals studied, suggesting that individual institutions have successfully reduced inappropriate prescribing. Interventions aimed at optimizing medication choice in the elderly after surgery – e.g. provider education,

computerized medication order entry alerts, and formulary restriction— could be implemented.²² These interventions, in conjunction with other processes of care aimed at optimizing surgical care in the elderly, could be used to develop standardized care protocols that could optimize care in the growing population of older surgical patients.

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Conflict of Interest Disclosures:

Elements of Financial/Personal Conflicts	Emily Finlayson		Judith Maselli		Michael Steinman		Michael Rothberg		Peter Lindenaier		Andrew Auerbach	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Employment or Affiliation		X		X		X		X		X		X
Grants/Funds		X		X		X		X		X		X
Honoraria		X		X		X		X		X		X
Speaker Forum		X		X		X		X		X		X
Consultant		X		X		X		X		X		X
Stocks		X		X		X		X		X		X
Royalties		X		X		X		X		X		X
Expert Testimony		X		X		X		X		X		X
Board Member		X		X		X		X		X		X
Patents		X		X		X		X		X		X
Personal Relationship		X		X		X		X		X		X

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Figure 1.
Distribution of PIM and Meperidine Prescribing Rates Among Hospitals Treating > 50 Surgical Patients.

Table 1**Patient and Provider Characteristics of Surgical Cohort**

Characteristic	Received PIM (n, %)	Did not receive PIM (n, %)	p-value
Age, mean (SD)	73.9 (6.3)	74.7 (6.4)	<0.001
Age group			<0.001
65-69	20919 (28.5%)	52492 (71.5%)	
70-74	18368 (26.2%)	51829 (73.8%)	
75-79	15691 (24.2%)	49102 (75.8%)	
80	14179 (22.2%)	49771 (77.8%)	
Gender			<0.001
Female	47032 (26.7%)	128860 (73.3%)	
Male	22125 (22.9%)	74334 (77.1%)	
Race/ethnicity			<0.001
White	52079 (25.5%)	152037 (74.5%)	
Black	3994 (24.1%)	12537 (75.8%)	
Hispanic	1817 (29.4%)	4362 (70.6%)	
Other	11267 (24.8%)	34258 (75.2%)	
Operation			<0.001
Gastrectomy	496 (20.8%)	1890 (79.2%)	
Ileostomy	126 (25.2%)	374 (74.8%)	
Colorectal resection	9418 (23.3%)	30982 (76.7%)	
Colostomy	205 (25.7%)	594 (74.3%)	
Nephrectomy	1536 (19.2%)	6479 (80.8%)	
Oophorectomy	619 (25.9%)	1773 (74.1%)	
Hysterectomy	2292 (21.8%)	8208 (78.2%)	
Knee arthroplasty	37630 (26.9%)	102328 (73.1%)	
Hip replacement	16835 (25.0%)	50566 (75.0%)	
Comorbid conditions			
COPD	11515 (27.3%)	30625 (72.7%)	<0.001
CHF	3925 (26.5%)	10888 (73.5%)	0.002
Valvular heart disease	3995 (23.7%)	12859 (76.3%)	<0.001
Pulmonary circulation disease	920 (25.9%)	2637 (74.1%)	0.515
Rheumatoid/collagen disorders	2392 (27.4%)	6337 (72.6%)	<0.001
Hypertension	48646 (25.4%)	142666 (74.6%)	0.519
Peripheral vascular disease	2468 (25.1%)	7383 (74.9%)	0.431
Neurological disease	2843 (26.6%)	7848 (73.4%)	0.004
Hypothyroidism	11811 (27.1%)	31833 (72.9%)	<0.001
Coagulopathy	1481 (26.5%)	4117 (73.5%)	0.065
Metastatic cancer	2043 (22.2%)	7155 (77.8%)	<0.001
Diabetes	14267 (25.2%)	42432 (74.8%)	0.158
Renal failure	3057 (23.5%)	9938 (76.5%)	<0.001
Deficiency anemia	13961 (26.5%)	38676 (73.5%)	<0.001

Characteristic	Received PIM (n, %)	Did not receive PIM (n, %)	p-value
Chronic blood loss anemia	2232 (26.4%)	6232 (73.6%)	0.036
Obesity	7698 (26.2%)	21675 (73.8%)	<0.001
Depression	6266 (27.6%)	16431 (72.4%)	<0.001
Weight loss	1267 (29.7%)	2997 (70.3%)	<0.001
Psychoses	961 (29.1%)	2346 (70.9%)	<0.001
Provider characteristics			
Location			<0.001
Rural	10446 (31.1%)	23099 (68.9%)	
Urban	58711 (24.6%)	180095 (75.4%)	
Area			<0.001
Midwest	5162 (14.0%)	31754 (86.0%)	
Northeast	14456 (23.0%)	48524 (77.0%)	
South	35368 (30.0%)	82354 (70.0%)	
West	14171 (25.9%)	40562 (74.1%)	
Teaching	11042 (18.8%)	47712 (81.2%)	<0.001
Not teaching	58115 (27.2%)	155482 (72.8%)	
Attending physician specialty			<0.001
General Surgery	9149 (21.6%)	33203 (78.4%)	
Urologic surgery	1452 (19.3%)	6066 (80.7%)	
Gynecologic surgery	2744 (22.5%)	9478 (77.5%)	
Orthopedic surgery	50008 (26.0%)	142441 (74.0%)	
Other*	5804 (32.6%)	12006 (67.4%)	
Consultation			<0.001
Non-surgeon consultation [†]	20408 (29.0%)	49914 (71.0%)	
Other or no consultation	48749 (24.1%)	153280 (75.9%)	

* Non-surgical specialties

[†] Internal medicine, hospitalist medicine, geriatric medicine, or family practice

Table 2

Frequency of PIM Use

Medication	Number of patients (%)
Any PIM	150,473 (55.3)
Always avoid	49,599 (18.2)
Meperidine	37,855 (13.9)
Belladonna alkaloids	8254 (3.0)
Trimethobenazamide	3703 (1.4)
Dicyclomine	728 (0.27)
Hyoscyamine	705 (0.26)
Flurazepam	263 (0.10)
Pentazocine	249 (0.09)
Meprobamate	45 (0.02)
Barbiturates	19 (0.01)
Chlorpropamide	17 (0.01)
Propantheline	13 (<0.01)
Rarely appropriate	24,985 (9.2)
Diazepam	8942 (3.3)
Cyclobenzaprine	8344 (3.1)
Propoxyphene	3834 (1.4)
Methocarbamol	2738 (1.0)
Carisoprodol	1019 (0.37)
Chlordiazepoxide	832 (0.3)
Metaxalone	648 (0.2)
Chlorzoxazone	76 (0.03)
Some indications	118,269 (43.4)
Diphenhydramine	59,967 (22.0)
Promethazine	52,027 (19.1)
Hydroxyzine	18,903 (6.9)
Amitriptyline	4999 (1.8)
Oxybutynin	2632 (1.0)
Indomethacin	956 (0.4)
Dipyridamole	897 (0.3)
Doxepin	775 (0.3)
Methyldopa	309 (0.1)
Cyproheptadine	142 (0.05)
Disopyramide	133 (0.05)
Chlorpheniramine	73 (0.03)
Ticlopidine	51 (0.02)
Reserpine	21 (0.01)

Table 3

Patient and Provider Characteristics Associated with Receipt of 'Always Avoid' and 'Rarely Appropriate' PIM in Multivariate Analysis.

Characteristic	Adjusted OR (95%CI)
Patient characteristics	
Age group	
65-69	Referent
70-74	0.89 (0.87, 0.91)
75-79	0.82 (0.79, 0.85)
80	0.71 (0.68, 0.74)
Gender	
Female	Referent
Male	0.83 (0.81, 0.85)
Race/ethnicity	
White	Referent
Black	0.80 (0.76, 0.85)
Hispanic	0.88 (0.81, 0.96)
Other	1.05 (0.98, 1.12)
Comorbid conditions	
Chronic obstructive pulmonary disease	1.09 (1.07, 1.12)
Congestive heart failure	1.08 (1.03, 1.14)
Rheumatoid/collagen disorders	1.08 (1.03, 1.14)
Hypothyroidism	1.05 (1.03, 1.07)
Diabetes	0.94 (0.92, 0.96)
Deficiency anemia	1.04 (1.01, 1.07)
Weight loss	1.24 (1.15, 1.34)
Psychoses	1.17 (1.09, 1.25)
Provider characteristics	
Geographic region	
Northeast	Referent
Midwest	1.40 (0.78, 2.47)
South	2.24 (1.38, 3.64)
West	1.79 (1.02, 3.16)
Attending physician specialty	
General Surgery	Referent
Urologic surgery	0.91 (0.82, 1.00)
Gynecologic surgery	0.94 (0.83, 1.05)
Orthopedic surgery	1.22 (1.08, 1.40)
Other*	1.40 (1.26, 1.55)
Non-surgeon consultation†	1.08 (1.02, 1.14)

* Non-surgical specialties

† Internal medicine, hospitalist medicine, geriatric medicine, or family practice