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ORIGINAL RESEARCH

Use of Oral Celecoxib Preoperatively Reduces Risk of Delirium and Favors Functional Recovery in Elderly Patients with Femoral Neck Fracture: A Propensity Score-Matched Analysis

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Background: We aim to explore whether the effect of oral celecoxib (OC) preoperatively in elderly patients with femoral neck fracture (FNF) receiving surgery on the pain control, complications, functional outcomes, and mortality.

Methods: We collected data on elderly patients with FNF in two hospitals between Jan. 2020 and May. 2024. According to OC use or not, patients were divided into OC group and non-OC group. We performed propensity score matching (PSM) analysis to minimize potential confounding and selection bias. We observed the factors that may influence pain control by Spearman correlations.

Results: Finally, 908 patients met our inclusion criteria, including 494 patients in the OC group and 414 in non-OC patients. We found that many factors, such as age, body mass index, and fracture type, were significantly different. Thus, we used PSM analysis to lower potential confounding, and 215 patients remained in each group. The results showed that VAS scores at the time of 1st day after surgery, 3rd day after surgery and at discharge were markedly lower in OC group. Additionally, lower delirium rate and better functional outcomes were found in OC group. Our finding showed no significant difference in mortality rates at 30-day, 90-day, and 12-month between two groups.

Conclusion: Preoperative OC can manage pain control, have better functional recovery, and minimize pain-related complications such as delirium in elderly patients with femoral neck fracture.

Level of Evidence: Level III.

Keywords: celecoxib, elderly, femoral neck fracture, pain, delirium

Introduction

With the intensification of the global aging population, approximately 100 million hip fractures require surgical treatment and comprehensive perioperative management every year, which poses a huge challenge to orthopedic doctors and also imposes a burden on the economies and medical resources of various countries. Ongoing evidence reports that the number of people more than 60 years old in China has reached 249 million, occupying nearly 20% of the total population by 2018.[1,2] It is expected that the elderly population will reach 450 million by 2050, accounting for over 30% of the global population by 2050.[1,2] Femoral neck fracture (FNF) is a common cause of mortality, immobility, and economic burden in the elderly due to various comorbidities and difficulties in postoperative recovery.[3–5] Despite significant improvements in current management, mortality still ranges from 26% to 37% with first-year follow-up.[6,7]

Pain management is an important part of perioperative management for the elderly with hip fractures. Increasing research has reported that pain control is closely related to post-operative outcomes, hospital stay, postoperative recovery, and even mortality.[8,9] Poor pain control is also associated with postoperative delirium, depressive symptoms and other adverse outcomes in older adults,[10,11] which may impair their daily lives, reduce their quality of life, and even increase

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mortality. Cyclooxygenase (COX)-2 inhibitors have acceptable gastrointestinal toxicity and are widely established for the clinical management of pain control.[12,13] Celecoxib, the first COX-2 inhibitor, is commonly utilized for relieving postoperative pain in hip surgeries and its potential mechanism.[14–18] However, related studies on the effect of using OC pre-operatively on postoperative delirium, mortality, and functional outcomes are relatively scarce. Our aim is to evaluate the effect of using preoperative OC in elderly patients with FNF on delirium and functional outcomes, as well as mortality.

Materials and Methods

Ethics Statement

The study was approved by the Institutional Review Board of affiliated hospital of Jiangnan University before data collection and analysis (LS2024039) in compliance with the Helsinki and an exemption from the informed consent was obtained. All data were anonymized before the analysis to safeguard patient privacy.

Patients

This retrospective study included FNF patients who received surgery between Jan. 2020 and May. 2024. According to using OC preoperatively (200mg QD) or not, patients were divided into OC group and non-OC group. All patients were treat with OC postoperatively (200mg QD). The inclusion criteria as follows: (1) patients with Garden III or IV type; (2) >60 years old; (3) no comorbidity was caused at the time of IF; (4) more than 1-year follow-up. The exclusion criteria were as follows: (1) patients with a history of hip fracture or hip surgery; (2) patients with open or pathological fractures; (3) patients with multiple injuries or fractures; (4) more than 48 hours since injury.

Data Collection

In the present study, we collected data, consisting of patient characteristics (age, gender, body mass index, BMI, residence, and a history of smoking or alcohol), injury-related data (fracture type, injury mechanism, and length of time from injury to admission), in-hospital data (American Society of Anesthesiologists, ASA, type of anesthesia, intraoperative blood loss, and duration of operation, Hb level at admission, blood transfusion, VAS at admission, VAS 1st day after surgery, VAS 3rd day after surgery, VAS at discharge, length of hospital stay, and deep vein thrombosis (DVT) at admission), comorbidities (coronary heart disease, heart failure, arrhythmia, hypertension, diabetes, myocardial infarction, cerebral hemorrhage, and cerebral infarction), complications after surgery (heart failure, respiratory failure, cerebral infarction, arrhythmia, pneumonia, delirium, anemia, DVT, electrolyte disturbance, and hypoproteinemia), and functional outcomes (independent walking, use of walking aids, use of wheelchair, bedridden, and death) as well as mortality (30-day mortality, 90-day mortality, and 12-month mortality).

Statistical Analysis

SPSS (version 27.0 SPSS Inc., Chicago, IL) was used with a significant level ($p<0.05$). For continuous variables, the Mann–Whitney *U*-test or *t*-test was performed according to whether the data met normality criteria or not. The chi-square test was employed for data analysis on count data. We performed propensity score matching (PSM) analysis based on the results of logistic regression analysis with a 1:1 ratio to adjust for discrepancies in baseline characteristics between the two groups to lower selection bias. After PSM, we used univariate regression analyses to observe the effect of OC on complications after surgery and functional outcomes, as well as mortality, then we investigated the association between VAS scores and other variables, such as age, gender, or BMI by Spearman correlation analysis.

Results

As shown in Figure 1, we collected 1211 patients with FNF in our hospital from Jan 2020 to May 2024. According to inclusion criteria and exclusion criteria, we removed 303 patients. Then, 908 patients, including 414 in non-OC group and 494 in OC group. Finally, 215 patients were included after PSM analysis.

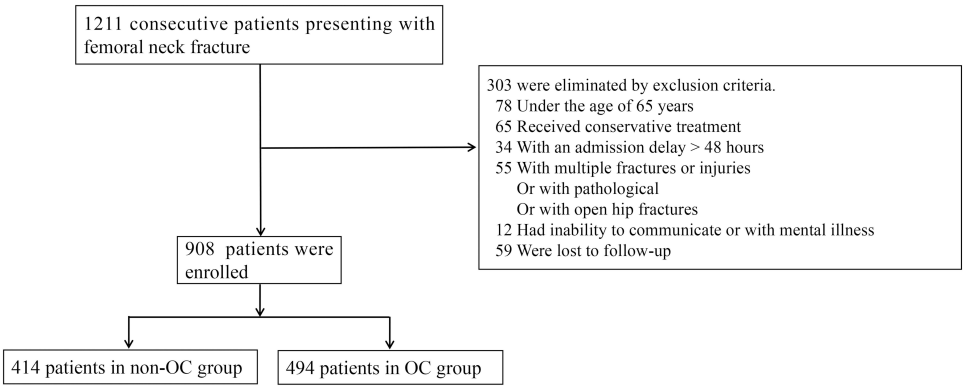

Figure 1 Flow diagram of included patients.

Before PSM analysis, there was no significant difference in gender, residence, injury type, time from injury to surgery, type of anesthesia, blood transfusion, VAS at admission, DVT at admission, patients with a history of smoking, drinking, hypertension, coronary heart disease, heart failure, arrhythmia, myocardial infarction, cerebral hemorrhage, or cerebral infarction between two groups. However, age ($p<0.001$), age group ($p=0.001$), BMI ($p=0.037$), Garden classification ($p<0.001$), ASA ($p<0.001$), Hb level at admission ($p<0.001$), VAS at admission (p=0.012) and a history of diabetes ($p=0.018$) were significant differences between the two groups before PSM analysis, but there was no marked difference after PSM analysis (Table 1).

Table 1 Comparisons of Patient Characteristics at Baseline Before and After Propensity Score Match

Variables	Pre-matching			Post-matching		
	OC group (n=494)	Non-OC group (n=414)	*P* value	OC group (n=215)	Non-OC group (n=215)	*P* value
Demographics						
Gender			0.787			0.43
Male	208	178		89	81	
Female	286	236		126	134	
Age, years	77.0±7.1	79.1±6.6	<0.001	79.4±7.2	79.1±7.6	0.73
Age group, *n*			0.001			0.719
60–69	69	33		17	24	
70–79	247	182		93	90	
80–89	155	175		85	81	
90–99	23	24		20	20	
BMI (kg/m^2)	24.1±2.7	24.5±3.4	0.037	24.2±3.1	24.5±3.1	0.322
Residence			0.891			0.381
Rural	260	216		126	117	
Urban	234	198		89	98	
Smoking history (Yes)	126	101	0.70	55	60	0.586
Drinking history (Yes)	98	94	0.292	43	48	0.555

(*Continued*)

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Table 1 (Continued).

Variables	Pre-matching			Post-matching		
	OC group (n=494)	Non-OC group (n=414)	*P* value	OC group (n=215)	Non-OC group (n=215)	*P* value
Injury-related data						
Garden classification			<0.001			0.499
III	268	210		107	100	
IV	226	284		108	115	
Injury type			0.216			0.326
Low energy	401	349		178	170	
High energy	93	65		37	45	
Time from injury to surgery, days	6.1±1.7	6.0±1.3	0.422	6.1±1.1	6.0±1.0	0.458
In-hospital data						
ASA			<0.001			0.832
1	79	78		36	30	
2	170	178		85	89	
3	181	137		78	82	
4	64	21		16	14	
Type of anesthesia, *n*			0.453			0.687
General anesthesia	159	143		78	74	
Regional anesthesia	335	271		137	141	
Hb level at admission (g/dL)			<0.001			0.981
≥ 12	99	97		51	48	
10–12	107	130		43	45	
8–10	150	146		66	65	
< 8	138	41		55	57	
Blood transfusion (Yes)	169	151	0.477	75	77	0.840
VAS at admission	5.9±1.3	6.1±1.0	0.012	6.0±1.2	6.1±1.1	0.248
DVT at admission	270	230	0.786	125	120	0.626
Comorbidities						
Hypertension, *n* (Yes)	191	156	0.761	88	92	0.696
Diabetes, *n* (Yes)	138	146	0.018	65	71	0.534
Coronary heart disease, *n* (Yes)	55	61	0.105	23	27	0.547
Heart failure, *n* (Yes)	34	31	0.725	15	13	0.696

(*Continued*)

Table 1 (Continued).

Variables	Pre-matching			Post-matching		
	OC group (n=494)	Non-OC group (n=414)	*P* value	OC group (n=215)	Non-OC group (n=215)	*P* value
Arrhythmia, *n* (Yes)	18	21	0.290	7	8	0.793
Myocardial infarction, *n* (Yes)	26	31	0.169	11	13	0.674
Cerebral hemorrhage, *n* (Yes)	36	41	0.159	14	16	0.705
Cerebral infarction, *n* (Yes)	38	43	0.156	15	17	0.713

Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; VAS, visual analog scores; DVT, deep vein thrombosis.

Table 2 and Figure 2 showed obviously lower VAS scores on the 1st day after surgery, 3rd day after surgery and at discharge in OC group, implying the important role of OC preoperatively in pain control after surgery. We then investigated the effect of OC preoperatively in elderly patients with FNF on complications, functional outcomes, as

Table 2 Patient Outcome Analyses After Propensity Score Matching

Variables	Postmatching		
	OC group (n=215)	Non-OC group (n=215)	*P* value
Duration of operation, mins	45.9±7.8	47.0±8.0	0.157
Intraoperative blood loss (mL)	100.0±19.6	105.2±14.6	0.002
VAS 1st day after surgery	3.1±0.8	4.3±1.1	<0.001
VAS 3rd day after surgery	2.2±0.7	3.1±0.8	<0.001
VAS at discharge	1.7±0.7	2.3±0.9	<0.001
Length of hospital stay, days	14.3±4.5	14.7±4.7	0.376
30-day mortality, n	2	2	1.00
90-day mortality, n	5	6	0.76
12-month mortality, n	8	10	0.630
Complications			
Heart failure, *n* (Yes)	2	3	1.00
Respiratory failure, *n* (Yes)	1	3	0.623
Cerebral infarction, *n* (Yes)	1	4	0.372
Arrhythmia, *n* (Yes)	2	2	1.00
Pneumonia, *n* (Yes)	4	3	1.00
Delirium, *n* (Yes)	3	12	0.032
Anemia, *n* (Yes)	56	65	0.334
DVT, *n* (Yes)	67	73	0.537
Electrolyte disturbance, *n* (Yes)	47	51	0.646
Hypoproteinemia, *n* (Yes)	55	58	0.742

(*Continued*)

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Table 2 (Continued).

Variables	Postmatching		
	OC group (n=215)	Non-OC group (n=215)	*P* value
Functional outcomes			
Independent walking	127	110	<0.001
Use of walking aids	57	34	
Use of wheelchair	13	30	
Bedridden	10	31	
Death	8	10	

Abbreviations: VAS, visual analog scores; DVT, deep vein thrombosis.

well as mortality. We found that the rate of delirium was significantly lower in OC group, but no close relationship between the use of OC and mortality. Spearman correlation analysis showed that OC preoperatively had the highest correlation with VAS scores at the time of 1st day after surgery and the lowest correlation with VAS scores at discharge (Table 3).

Discussion

Based on previous research, almost two-thirds of patients experienced moderate-to-severe pain before surgery,[19,20] yet over 70% of patients still do not receive pain management.[19] To our knowledge, various factors, including poor treatment compliance, concerns about side effects, and inconsistent prescription practices among clinicians, contribute to inconsistent and insufficient pain management.[21] Pain management is of utmost importance in the perioperative management of elderly hip fractures, and it is also a huge challenge for clinicians. Poor pain control can lead to many adverse consequences, such as anxiety, poor postoperative function recovery, and even increased mortality.

Guo[21] has explored the effect of intravenous paracetamol preoperatively in older patients with intertrochanteric fractures on the reverse events and found the beneficial effects of intravenous paracetamol preoperatively on pain control, pain-related complications, and functional recovery. Increasing evidence has reported the good safety and efficacy of treatment with the COX2-selective inhibitor, celecoxib, in pain management of femoral head necrosis, knee and hip osteoarthritis.[22–24] To date, no study has investigated the efficacy of OC preoperatively on delirium and functional outcomes, as well as mortality in patients with FNF.

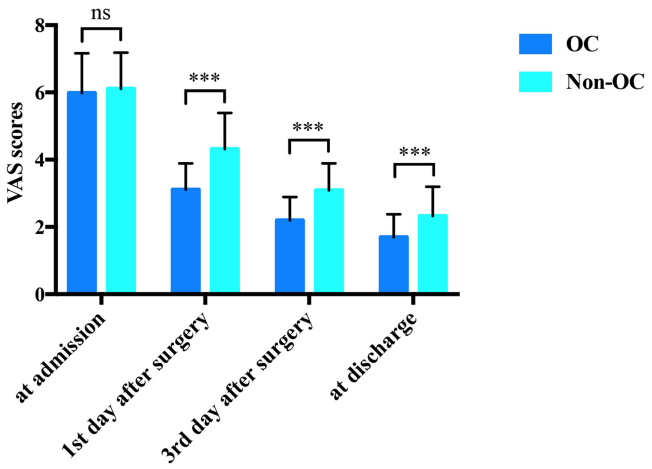

Figure 2 VAS score at different times in two groups (ns: no significant; ***: <0.0001).

Table 3 The Association of VAS Scores with Other Variables

Variables	VAS at Admission	*p* value	VAS 1st Day After Surgery	*p* value	VAS 3rd Day After Surgery	*p* value	VAS at Discharge	*p* value
Gender	0.01	0.832	0.02	0.68	0.034	0.484	−0.057	0.242
Age	−0.009	0.848	0.023	0.635	−0.116	0.016	0.054	0.26
BMI	−0.008	0.869	−0.035	0.47	−0.075	0.123	−0.007	0.888
Residence	−0.073	0.128	0.049	0.312	0.05	0.303	0.074	0.128
Smoking history (Yes)	0.003	0.952	−0.042	0.385	0.022	0.646	−0.096	0.047
Drinking history (Yes)	−0.039	0.417	−0.069	0.151	−0.026	0.589	−0.055	0.252
Garden classification	−0.022	0.649	0.034	0.488	0.003	0.955	0.026	0.592
Injury type	0.062	0.200	0.047	0.329	0.096	0.047	−0.077	0.11
ASA	0.296	0.046	−0.008	0.862	−0.006	0.896	−0.031	0.52
OC	NA	NA	0.558	<0.001	0.525	<0.001	0.359	<0.001

Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; VAS, visual analog scores; OC,Oral Celecoxib.

Therefore, we conducted a retrospective study to explore the effect of OC preoperatively in patients with FNF with 12-month follow-up by PSM analysis. Before PSM analysis, age, age group, BMI, Garden classification, ASA, Hb level at admission, and a history of diabetes were significantly different in two groups, but there was no marked difference after PSM analysis. Then, we found that VAS scores at the time of the 1st day after surgery, the 3rd day after surgery, and at discharge were markedly lower in OC group. Additionally, a lower delirium rate and better functional outcomes were found in OC group. Our findings showed no significant difference in mortality at 30-day, 90-day, and 12-month between the two groups.

Prior research has reported that pain management was correlated with length of hospital stay or even mortality.[8,9] However, Guo[21] did not find a close relationship between pain control and function recovery and even mortality, which was similar to our findings. In our study, 4.2% (18 of 430) of all patients died at the final follow-up, and the mortality of the non-OC group and OC group in 12 months were 3.7% and 4.6% after PSM, respectively, which was significantly lower than previous data.[25,26] This may be related to the race of the subjects or a distinct fracture. Furthermore, we found 85.6% (127 patients with independent walking and 57 patients with walking aids) of patients receiving OC preoperatively obtained good function recovery, while 67.0% (110 patients with independent walking and 34 patients with walking aids) of patients without OC preoperatively achieved good function recovery.

Previous research has reported that poor pain control can cause some adverse events, such as postoperative complications, depressive symptoms, and other outcomes in older adults,[10,11] which may reduce their quality of life, and even increase mortality. Therefore, pain control during the perioperative period plays a crucial role in reducing adverse events in older patients with FNF. In our study, OC preoperatively can dramatically reduce VAS scores from 6.0 points at admission to 3.1 points at the 1st day after surgery, 2.2 points at the 3rd day after surgery, and 1.7 points at discharge, which is markedly lower than in non-OC group. Our findings implied that OC preoperatively is an effective management. Additionally, we used Spearman correlation analysis to find that OC preoperatively had the highest correlation with VAS scores at the time of 1st day after surgery and the lowest correlation with VAS scores at discharge.

We also compare the rate of complications after surgery in two groups. We first matched comorbidities in two groups using PSM analysis, which can lower the potential confounding biases. Surprisingly, only the rate of postoperative delirium was significantly lower in OC group and in non-OC group, but there was no obvious difference in other

complications, such as heart failure, and diabetes. To the best of our knowledge, postoperative delirium is a relatively rare complication after hip surgery, but it is a main cause for mortality after surgery. According to prior research, the rate of delirium was over 50% after hip fracture repair.[27–30] Poor pain control is also associated with postoperative delirium,[10,11] implying that pain control is an important role in preventing delirium.

To our knowledge, this is the first study to evaluate the functional outcomes of OC preoperatively in patients with FNF after PSM analysis. This quantitative analysis may improve the confidence of orthopedic surgeons in pain control for patients with FNF and be beneficial for clinicians to seek the possibility of establishing future outcomes of adverse functions, and to establish reasonable medical care goals for this vulnerable population. However, one drawback is that it is a retrospective, single-center observational study. In addition, we did not exclude other unknown factors, such as the laboratory indicators during the perioperative period, for analysis, which may affect our results.

In conclusion, regarding FNF patients with moderate-to-severe pain, using preoperative OC can be more likely to relieve pain, reduce pain-related complications like delirium, and obtain better functional recovery. Our findings underline that preoperative OC can help clinicians and nursing staff effectively control pain and its related complications.

Data Sharing Statement

The original contributions presented in the study are included in the article; further inquiries can be directed to the corresponding authors.

Ethics Approval and Consent to Participate

The study was approved by the Institutional Review Board of affiliated hospital of Jiangnan university before data collection and analysis (LS2024039) in compliance with the Helsinki and an exemption from the informed consent was obtained. All data were anonymized before the analysis to safeguard patient privacy.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare no competing interests in this work.

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