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ผลลัพธ์ทางคลินิกและต้นทุนการรักษาที่สัมพันธ์กับการให้คีโตโรแลคทางหลอดเลือดดำภายหลังการผ่าตัดเชื่อมข้อกระดูกสันหลังส่วนเอว: การศึกษาแบบย้อนหลัง

Clinical and Economic Outcomes Associated With Postoperative Intravenous Ketorolac Use After Posterolateral Lumbar Fusion: A Retrospective Cohort Study

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บทคัดย่อ

หลักการและเหตุผล : การให้ ketorolac ทางหลอดเลือดดำเป็นส่วนหนึ่งของการระงับปวดแบบหลายวิธีภายหลังการผ่าตัดเชื่อมข้อกระดูกสันหลังส่วนเอว อย่างไรก็ตาม ยังมีข้อมูลจำกัดเกี่ยวกับผลลัพธ์ทางคลินิกและต้นทุนการรักษาในผู้ป่วยกลุ่มนี้

วัตถุประสงค์ : เพื่อเปรียบเทียบผลลัพธ์ทางคลินิกและต้นทุนการรักษาระหว่างผู้ป่วยที่ได้รับ ketorolac ทางหลอดเลือดดำ ภายหลังการผ่าตัดเชื่อมข้อกระดูกสันหลังส่วนเอวกับผู้ป่วยที่ไม่ได้รับ ketorolac

วิธีการศึกษา : เป็นการศึกษาแบบย้อนหลัง โดยการทบทวนเวชระเบียนผู้ป่วยที่ได้รับการผ่าตัดเชื่อมข้อกระดูกสันหลังส่วนเอว ณ โรงพยาบาลสุรินทร์ ระหว่างวันที่ 1 มกราคม พ.ศ. 2563 ถึง 31 ธันวาคม พ.ศ. 2568 เปรียบเทียบผู้ป่วยที่ได้รับ ketorolac ทางหลอดเลือดดำ ขนาด 30 มิลลิกรัม ทุก 12 ชั่วโมง หลังผ่าตัด กับผู้ป่วยที่ไม่ได้รับ ketorolac ผลลัพธ์ที่ศึกษา ได้แก่ คะแนนความปวดหลังผ่าตัด การเสียเลือด ระยะเวลานอนโรงพยาบาล และต้นทุนการรักษา

ผลการศึกษา : ผู้ป่วยทั้งหมด 127 ราย แบ่งเป็นกลุ่มที่ได้รับ ketorolac 82 ราย และกลุ่มควบคุม 45 ราย หลังปรับปัจจัยกวน ไม่พบความแตกต่างของคะแนนความปวดเฉลี่ยหลังผ่าตัด การเสียเลือดระหว่างผ่าตัด และปริมาณเลือดจากสายระบาย อย่างไรก็ตาม กลุ่มที่ได้รับ ketorolac มีระยะเวลานอนโรงพยาบาลหลังผ่าตัดสั้นกว่า 0.88 วัน p = 0.049 และมีต้นทุนการรักษารวมต่ำกว่า 8,299 บาท p = 0.002 อย่างมีนัยสำคัญทางสถิติ

สรุป : การให้ ketorolac ทางหลอดเลือดดำระยะสั้นภายหลังการผ่าตัดเชื่อมข้อกระดูกสันหลังส่วนเอว ไม่พบความแตกต่างอย่างมีนัยสำคัญของคะแนนความปวดหรือการเสียเลือด แม้พบระยะเวลานอนโรงพยาบาลหลังผ่าตัดที่สั้นกว่าและต้นทุนการรักษาที่ต่ำกว่า แต่ความสัมพันธ์ดังกล่าวควรตีความด้วยความระมัดระวังเนื่องจากข้อจำกัดของการศึกษาแบบย้อนหลัง

คำสำคัญ : คีโตโรแลค การผ่าตัดเชื่อมข้อกระดูกสันหลังส่วนเอว คะแนนความปวด ระยะเวลานอนโรงพยาบาล ต้นทุนการรักษา

ABSTRACT

Background : Intravenous ketorolac is commonly used as part of multimodal analgesia following posterolateral lumbar fusion. However, evidence regarding its clinical and economic outcomes in patients undergoing posterolateral lumbar fusion remains limited.

Objective : To compare the clinical and economic outcomes between patients who received postoperative intravenous ketorolac and those who did not receive ketorolac following posterolateral lumbar fusion.

Methods : A retrospective cohort study was conducted by reviewing medical records of patients who underwent lumbar fusion surgery at Surin Hospital between 1st. January 2020 and 31st. December 2025. Patients who received intravenous ketorolac 30 mg every 12 hours postoperatively were compared with those who did not receive ketorolac. Outcomes of interest included postoperative pain scores, blood loss, length of hospital stay, and treatment costs.

Results : A total of 127 patients were included in the study, comprising 82 patients in the ketorolac group and 45 patients in the control group. After adjustment for potential confounders, no significant differences were observed in postoperative pain scores, intraoperative blood loss, or postoperative drain output. However, the ketorolac group had a significantly shorter postoperative length of stay by 0.88 days $p = 0.049$ and lower total treatment costs by 8,299 THB $p = 0.002$ compared with the control group.

Conclusions : Short-course postoperative intravenous ketorolac after posterolateral lumbar fusion was not associated with significant differences in postoperative pain or blood loss. Although shorter postoperative hospitalization and lower treatment costs were observed, these associations should be interpreted cautiously given the retrospective study design.

Keywords : Ketorolac, Posterolateral Lumbar Fusion Surgery, Pain Score, Length of Stay, Treatment Cost.

Background

Lumbar spinal fusion is a common procedure for the treatment of degenerative lumbar spine disorders. Despite advances in surgical techniques and perioperative care, postoperative pain remains a major challenge, delaying mobilization, prolonging hospital length of stay (LOS), increasing opioid consumption, and increasing healthcare costs. Consequently, multimodal analgesia has become a key component of Enhanced Recovery After Surgery (ERAS) pathways for lumbar fusion.[1]

Ketorolac, a nonsteroidal anti-inflammatory drug (NSAID), is widely used as part of multimodal analgesia because of its analgesic and opioid-sparing effects. A recent systematic review and meta-analysis demonstrated that perioperative ketorolac significantly reduced postoperative pain, opioid consumption,

and hospital LOS without increasing short-term complications.[2] A randomized controlled trial similarly reported reductions in opioid use and LOS following lumbar fusion.[3] However, concerns regarding renal toxicity, bleeding, cardiovascular events, and impaired spinal fusion have limited its routine use. Current evidence suggests that short-term, standard-dose ketorolac does not increase nonunion risk, whereas high-dose or prolonged administration may increase pseudarthrosis.[4-7]

In routine clinical practice, ketorolac is frequently administered at lower doses together with other perioperative interventions, including dexamethasone, tranexamic acid, and thromboprophylaxis,[8] making its independent clinical benefit uncertain. Furthermore, previous studies have mainly focused on pain control and opioid consumption, whereas evidence regarding healthcare utilization and treatment costs remains limited.

Objective

Therefore, this study evaluated the clinical and economic outcomes of low-dose postoperative intravenous ketorolac (30 mg every 12 hours, up to two doses) in patients undergoing posterolateral lumbar fusion in a real-world clinical setting. Primary outcomes included postoperative pain, whereas secondary outcomes included blood loss, hospital LOS, and treatment costs.

Methods

Study Design

This retrospective cohort study was conducted at Surin Hospital, Thailand. Medical records of patients who underwent posterolateral lumbar fusion (PLF) for degenerative lumbar spine disorders between January 1st., 2020, and December 31th., 2025, were reviewed. This study was approved by the Human Research Ethics Committee of Surin Hospital, with the approval number 32/2569, dated June 28th., 2026.

Study Population

Patients aged ≥18 years who underwent PLF for degenerative lumbar spinal stenosis, lumbar disc herniation, spondylolisthesis, or degenerative scoliosis were eligible. Patients were excluded if they had surgery for trauma, infection, tumor, or other non-degenerative conditions, incomplete medical records, end-stage renal disease (estimated glomerular filtration rate ≤30 mL/min/1.73 m²), documented NSAID allergy, major perioperative neurological complications requiring reoperation, or missing baseline hemoglobin values.

Exposure

Patients were classified according to postoperative intravenous ketorolac administration. The ketorolac group received 30 mg intravenously every 12 hours for up to two doses during the first 24 hours after surgery, whereas the control group did not receive postoperative ketorolac.

Perioperative management followed routine institutional practice and was not standardized for this retrospective study. Concomitant medications potentially affecting postoperative pain or perioperative bleeding were recorded, including preemptive analgesia, dexamethasone, tranexamic acid, and enoxaparin. The use of these medications was determined by the treating surgeons and anesthesiologists. Tranexamic acid, dexamethasone, and

enoxaparin were included as covariates in the adjusted analyses to account for their potential confounding effects.

Data Collection and Outcomes

Demographic, clinical, and perioperative data were extracted from electronic medical records, including age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status, diagnosis, number of fused levels, preoperative hemoglobin, estimated glomerular filtration rate (eGFR), international normalized ratio (INR), operative time, estimated blood loss, and perioperative medication use. For statistical adjustment, diagnoses were categorized as non-complex degenerative disease (lumbar spinal stenosis or lumbar disc herniation) or complex degenerative disease (spondylolisthesis, degenerative scoliosis, cauda equina syndrome, or revision surgery).

The primary outcome was the mean postoperative visual analogue scale (VAS) pain score during postoperative days (POD) 1-3. Secondary outcomes included VAS scores on POD1-3, intraoperative blood loss, postoperative drain output, blood transfusion requirement, duration of drain placement, total and postoperative length of stay (LOS), and treatment costs, including room, drug and miscellaneous medical, instrument, and total hospital costs.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD) or median (interquartile range), and categorical variables as frequencies and percentages. Baseline characteristics were compared using standardized mean differences (SMD) together with appropriate parametric or nonparametric tests. The primary analysis used multivariable regression models adjusted for prespecified confounders, including age, sex, preoperative hemoglobin, diagnosis group, number of fused levels, tranexamic acid use, dexamethasone use, and enoxaparin use. Linear regression was used for continuous outcomes, whereas treatment costs were analyzed using generalized linear models with a gamma distribution and log-link function.

Sensitivity analyses included a fully adjusted model that additionally incorporated BMI, eGFR, INR, surgeon, and dexamethasone treatment category. To further minimize treatment-selection bias, inverse probability of treatment weighting (IPTW) and doubly robust analyses were performed. Effect estimates are reported as regression coefficients (β) with 95% confidence intervals (CI). Statistical significance was defined as a two-sided $p < 0.05$. Complete-case analysis was performed, and patients with missing baseline covariates were excluded from multivariable analyses.

Results

A total of 127 patients were included (82 ketorolac and 45 controls). Although baseline characteristics were generally similar, clinically important imbalances were observed in age, preoperative hemoglobin, fused levels, and perioperative medication use (Table 1). These differences were addressed using multivariable regression and propensity score–based analyses.

Table 1: Baseline Characteristics of Patients (n=127)

Characteristics	Ketorolac group (n=82)	Control group (n=45)	p-value	SMD
Age (years)	60.5 ± 7.0	56.6 ± 9.2	0.02*	0.47
Female sex	46 (56.1%)	19 (42.2%)	0.19	0.28
BMI (kg/m²)	23.4 ± 4.2	24.8 ± 5.1	0.12	-0.30
ASA 3	65 (79.3%)	33 (73.3%)	0.59	0.14
Preoperative Hb (g/dL)	12.0 ± 1.5	12.7 ± 1.3	0.003*	-0.55
eGFR (mL/min/1.73m²)	85.3 ± 18.3	89.7 ± 19.7	0.22	-0.23
INR	1.05 ± 0.1	1.03 ± 0.1	0.27	0.21
Number of fused levels	2.3 ± 1.0	2.7 ± 1.4	0.06	-0.37
≥ 3 fused levels	26 (31.7%)	23 (51.1%)	0.03*	0.40
Operative time (min)	164.8 ± 45.5	168.0 ± 58.0	0.75	-0.06
Diabetes mellitus	14 (17.1%)	5 (11.1%)	0.52	0.17
Hypertension	26 (31.7%)	11 (24.4%)	0.51	0.16
Dyslipidemia	5 (6.1%)	3 (6.7%)	1.00	-0.02
Complex diagnosis	7 (8.5%)	7 (15.6%)	0.36	-0.22
TXA use	78 (95.1%)	26 (57.8%)	<0.001*	0.98
Dexamethasone Use	81 (98.8%)	34 (75.6%)	<0.001*	0.69
Intraoperative dexamethasone	73 (89.0%)	12 (26.7%)	<0.001*	1.63
Postoperative dexamethasone	80 (97.6%)	32 (71.1%)	<0.001*	0.78
Enoxaparin use	4 (4.9%)	16 (35.6%)	<0.001*	-0.76
Postoperative enoxaparin	2 (2.4%)	4 (8.9%)	0.23	-0.28
Preemptive analgesia	70 (85.4%)	14 (31.1%)	<0.001*	1.32

* p-value < 0.05

After adjustment for prespecified confounders, postoperative intravenous ketorolac was associated with significantly shorter postoperative length of stay and lower total treatment costs. Although postoperative pain scores were consistently lower in the ketorolac group, the differences were not statistically significant. No significant differences were observed in intraoperative blood loss, postoperative drain output, or total hospital length of stay. Similar findings for treatment costs were observed using gamma generalized linear models (Table 2).

Table 2: Clinical outcome primary adjusted model (Adjusted for age, sex, pre-op Hb, diagnosis group, fused levels, TXA, dexamethasone, enoxaparin).

Outcome	β	95% CI	p-value
Mean VAS POD1-3	-0.54	-1.15 to 0.06	0.08
VAS POD1	-0.60	-1.33 to 0.14	0.11
VAS POD2	-0.55	-1.33 to 0.23	0.17
VAS POD3	-0.49	-1.18 to 0.20	0.16
Intraoperative blood loss (ml)	-103	-313 to 107	0.33
Postoperative blood loss (ml)	-92	-220 to 36	0.16
Total LOS (days)	-0.96	-2.07 to 0.14	0.09
Post-op LOS (days)	-0.88	-1.76 to -0.01	0.049*
Total cost (Baht)	-8,299	-13,489 to -3,109	0.002*
Cost ratio, Gamma GLM	0.91	0.86 to 0.96	<0.001*

* p-value < 0.05

Sensitivity analyses demonstrated similar effect estimates to the primary analysis, although statistical significance differed for some outcomes (Supplementary Tables S2, S3, and S5).

Table 3: Adjusted Economic Outcomes Associated with Postoperative Intravenous ketorolac Use (Adjusted for age, sex, preoperative hemoglobin, diagnosis group, number of fused levels, tranexamic acid use, dexamethasone use, and enoxaparin use.)

Cost	Adjusted β	95% CI	p-value
Room cost (Baht)	-445	-940 to 50	0.078
Instrument cost (Baht)	220	-2,355 to 2,796	0.867
Drug and other cost (Baht)	-8,074	-12,127 to -4,022	<0.001*
Total cost (Baht)	-8,299	-13,435 to -3,163	0.002*

* p-value < 0.05

After adjustment for potential confounders, postoperative intravenous ketorolac use was associated with lower total treatment costs. The difference was primarily observed in the drug and other medical cost, whereas room and instrument-related costs did not differ significantly between groups (Table 3). However, the available cost data did not allow further identification of the specific components responsible for the difference in drug and other medical costs.

DISCUSSION

The present study evaluated the clinical and economic outcomes of postoperative intravenous ketorolac following posterolateral lumbar fusion in routine clinical practice. After adjustment for confounding factors, ketorolac was associated with a shorter postoperative length of stay and lower treatment costs, whereas postoperative pain scores showed a consistent but nonsignificant reduction in the primary analysis. The results of sensitivity analyses were generally consistent with the primary analysis (Supplementary Tables S3 and S5), supporting the robustness of the findings.

The analgesic effect of ketorolac was modest. Mean VAS during postoperative days 1-3 was reduced by 0.54 points in the primary analysis and by 0.49 points in the doubly robust analysis. These reductions were smaller than those reported in recent randomized trials and meta-analyses, which demonstrated the greatest benefit during the first 12 postoperative hours.[2,3] This difference may be explained by the later timing of pain assessment in our study, the use of a low-dose regimen (30 mg intravenously every 12 hours for up to two doses), and the concurrent administration of dexamethasone, tranexamic acid, and preemptive analgesia. Although the unadjusted analysis showed a 1-point reduction in VAS on postoperative day 1, this effect was attenuated after adjustment for baseline imbalances. This finding suggests that baseline confounding, particularly differences in perioperative medication use, may have attenuated the observed treatment effect after adjustment.

The reduction in postoperative length of stay appears clinically important. Ketorolac shortened postoperative hospitalization by 0.88 days in the primary analysis and by

approximately 1.3-1.4 days in the IPTW and doubly robust analyses, exceeding the pooled reduction of 0.45 days reported in a recent meta-analysis.[2] Differences in discharge practice, perioperative protocols, and healthcare systems may partly explain this larger effect observed in our real-world setting.

The economic analysis showed that ketorolac use was associated with lower adjusted total treatment costs of 8,299, 11,160, and 12,162 Thai baht in the primary, fully adjusted, and doubly robust analyses, respectively. The observed differences were mainly attributable to lower drug and other medical costs, whereas instrument-related costs were unchanged. Ketorolac used in our institution was a generic product supplied through the hospital procurement system. However, the available cost data did not allow further identification of the specific medications or healthcare resources responsible for the lower drug and other medical costs. Therefore, the observed difference in total treatment costs cannot be directly attributed to ketorolac administration and may reflect differences in other medications, length of stay, healthcare utilization, or other unmeasured factors.

Importantly, this study did not directly compare the cost of ketorolac with other NSAIDs or COX-2 inhibitors. Therefore, these findings should not be interpreted as evidence that ketorolac is more cost-effective than alternative analgesic agents. Although previous studies have primarily focused on pain control, opioid consumption, complications, and fusion outcomes,[2,3] further prospective studies with standardized perioperative analgesic protocols and detailed cost analyses are needed to determine the economic impact of ketorolac compared with other analgesic strategies.

This study has several strengths. It reflects real-world clinical practice, evaluated both clinical and economic outcomes, adjusted for major confounders, and incorporated sensitivity analyses to strengthen the validity of the findings.

Limitations

Several limitations should be acknowledged. First, the retrospective design cannot eliminate residual confounding. Second, treatment allocation was non-randomized, and important baseline differences existed in perioperative medication use. Although tranexamic acid, dexamethasone, and enoxaparin were included in the adjusted analyses, residual confounding from other medications affecting pain or bleeding cannot be excluded. Third, postoperative analgesic regimens were not standardized, and detailed postoperative opioid consumption was unavailable, which may have influenced the observed pain outcomes. Fourth, the study may have been underpowered to detect the modest reduction in pain scores observed after adjustment. Finally, this study included only patients undergoing posterolateral lumbar fusion. Therefore, the findings may not be directly generalizable to patients undergoing interbody fusion procedures such as PLIF, TLIF, OLIF, or ALIF.

Recommendations

Future prospective randomized trials should evaluate standardized low-dose ketorolac protocols with assessment of opioid consumption, functional recovery, patient-reported outcomes, cost-effectiveness, and one-year radiographic fusion. Based on the observed effect size for mean VAS during POD1-3, a future randomized controlled trial would require approximately 110 patients per group to detect a 0.5-point difference with 80% power and a two-sided alpha of 0.05. Allowing for missing data, approximately 245 patients should be enrolled.

Conclusions

In conclusion, short-course postoperative intravenous ketorolac (30 mg every 12 hours for up to two doses) after posterolateral lumbar fusion was not associated with significant differences in postoperative pain or perioperative blood loss. Further prospective controlled studies are needed to evaluate its clinical and economic effects.

Reference

1. Debono B, Wainwright TW, Wang MY, Sigmundsson FG, Yang MMH, Smid-Nanninga H, et al. Consensus statement for perioperative care in lumbar spinal fusion: Enhanced Recovery After Surgery (ERAS®) Society recommendations. Spine J 2021;21(5):729-52. doi: 10.1016/j.spinee.2021.01.001.
2. Guan J, Feng N, Yang K, Abudouaini H, Liu P. The efficacy and safety of ketorolac for postoperative pain management in lumbar spine surgery: a meta-analysis of randomize d controlled trials. Syst Rev 2024;13(1):275. doi: 10.1186/s13643-024-02685-z.
3. Iyer S, Steinhaus ME, Kazarian GS, Zgonis EM, Cunningham ME, Farmer JC, et al. Intravenous Ketorolac Substantially Reduces Opioid Use and Length of Stay After Lumbar Fusion: A Randomized Controlled Trial. Spine (Phila Pa 1976) 2024;49(2):73-80. doi: 10.1097/BRS.0000000000004831.
4. Li Q, Zhang Z, Cai Z. High-dose ketorolac affects adult spinal fusion: a meta-analysis of the effect of perioperative nonsteroidal anti-inflammatory drugs on spinal fusion. Spine (Phila Pa 1976) 2011;36(7):E461-8. doi: 10.1097/BRS.0b013e3181dfd163.
5. Glassman SD, Rose SM, Dimar JR, Puno RM, Campbell MJ, Johnson JR. The effect of postoperative nonsteroidal anti-inflammatory drug administration on spinal fusion. Spine (Phila Pa 1976) 1998;23(7):834-8. doi: 10.1097/00007632-199804010-00020.
6. Park JB, Cho YS, Riew KD. Development of postoperative nonunion associated with ketorolac use after posterolateral lumbar fusion. Spine (Phila Pa 1976) 2005;30(21):2432-7. doi:10.1097/01.brs.0000184684.95713.88
7. Li J, Ajiboye RM, Orden MH, Sharma A, Drysch A, Pourtaheri S. The Effect of Ketorolac on Thoracolumbar Posterolateral Fusion: A Systematic Review and Meta-Analysis. Clin Spine Surg 2018;31(2):65-72. doi: 10.1097/BSD.0000000000000613.