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Association of Liposomal Bupivacaine With Opioid Use and Medical Costs Following Surgery of Lower Extremity Fractures in Medicare Fee-for-Service Beneficiaries

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OBJECTIVE

To evaluate the impact of liposomal bupivacaine (LB) on opioid prescriptions and healthcare costs 30 days after lower extremity procedures in Medicare Fee-for-Service beneficiaries.

CONCLUSIONS

1. Medicare-insured patients receiving LB for outpatient lower extremity fracture procedures experienced fewer opioid-treated days, a lower opioid-related adverse event (ORAE) rate, and lower all-cause total medical cost over 30 days after surgery versus those who received non-LB analgesia
2. These data support the clinical and economic benefits of LB for postoperative pain management in lower extremity procedures

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REFERENCES: 1. Keene et al. *Bone Joint J.* 2021;103-B(6):1047-1054. **2.** Shields et al. *Eur J Orthop Surg Traumatol.* 2022;32(4):719-723. **3.** Joshi et al. *J Clin Anesth.* 2016;35:524-529. **4.** Wang et al. *J Foot Ankle Surg.* 2015;54(4):625-635. **5.** LaRowe et al. *Transl Behav Med.* 2025;15(1):ibaf048.

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INTRODUCTION

- It is essential to recognize the potential for chronic neuropathic pain development and ensure optimal pain management after lower extremity fracture procedures[1]
  - These procedures are shifting to outpatient from inpatient settings to lower hospital costs and shorten the length of hospital stays for patients[2]
- Pain management for lower extremity procedures via peripheral nerve blocks is associated with reductions in opioid prescriptions and AEs after surgery[3,4]
- The NOPAIN Act has recently expanded reimbursement for qualifying nonopioid therapies, including LB, when used for outpatient procedures in Medicare-insured patients[5]
  - However, clinical and economic data on LB use for outpatient lower extremity fracture procedures in Medicare-insured patients are limited

METHODS

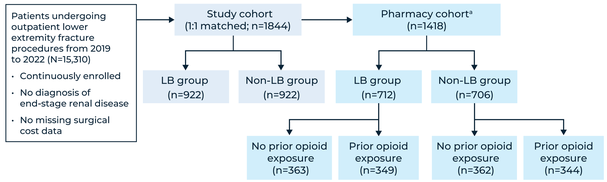
- In this retrospective, real-world cohort study, data on adult patients undergoing lower extremity procedures for fractures of the tibia, fibula, ankle, and foot between 2019 and 2022 with or without LB in hospital outpatient department settings were sourced from the 20% Centers for Medicare & Medicaid Services-Medicare database (Parts A, B, and D; database review year range, 2018-2023)
- Exclusion criteria were lack of continuous enrollment, end-stage renal disease diagnosis, inpatient surgery, and lack of surgical cost data
- The LB and non-LB groups were generated with 1:1 propensity score (PS) matching based on 14 baseline covariates
- Outcomes included
  - Cumulative opioid prescriptions (in morphine milligram equivalents [MMEs]), duration of use, and ORAEs, measured over the 30 days after surgery
  - Total medical costs, measured over the 30 days after discharge
    - Distinct categories included inpatient, emergency department, and outpatient costs
- Comparisons between groups for the study outcomes were performed via generalized linear regression with Gamma, Tweedie, negative binomial, or binomial distributions, as appropriate
  - Prior opioid exposure (defined as the filling of any opioid prescription within 6 months before the surgery date [as reported by their Medicare plan]) was used for subgroup analysis

RESULTS

PATIENT CHARACTERISTICS AND DEMOGRAPHICS AT SCREENING

- In total, 1844 patients (922 in the LB and non-LB groups, respectively) were included (Figure 1)
  - A separate pharmacy cohort included patients with Medicare Part D coverage and was used for analysis of cumulative opioid prescriptions, duration of use, and ORAEs

Figure 1. Cohort for retrospective analysis.



[a]Included patients with Medicare Part D coverage. LB, liposomal bupivacaine.

- Patient characteristics were balanced between groups after PS matching (standardized mean difference, <15%; patients had a mean age of 72 years, 71% were female, 91% were White, and 51% had osteoarthritis) (Table 1)
  - Approximately half the cohort (49%) had prior opioid exposure

Table 1. Baseline Characteristics in Patients Undergoing Lower Extremity Procedures in Hospital Outpatient Department Settings From 2019 to 2022

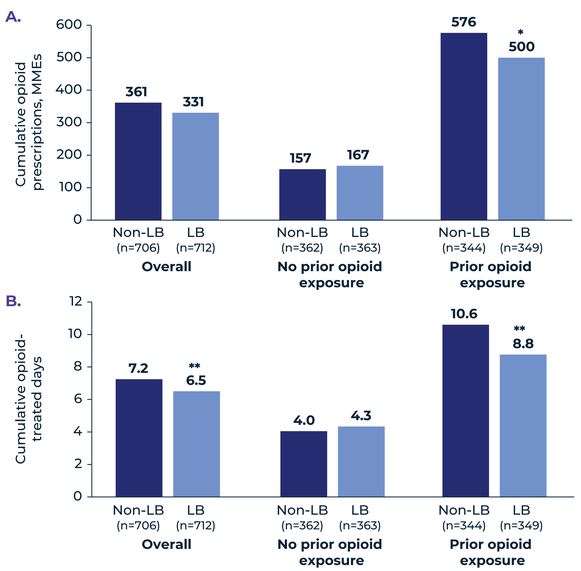
Baseline characteristics	PS-matched LB group (n=922)	PS-matched non-LB group (n=922)	PS-matched SMD, %
Age, mean (SD), y	71.72 (9.10)	71.60 (9.98)	1.26
Female, n (%)	656 (71.15)	651 (70.61)	1.19
White, n (%)	841 (91.21)	841 (91.21)	0.00
Region, n (%)			
Northeast	147 (15.94)	134 (14.53)	3.92
Midwest	216 (23.43)	213 (23.10)	0.77
South	409 (44.36)	431 (46.75)	-4.79
West	149 (16.16)	144 (15.62)	1.48
CCI, mean (SD)	0.94 (1.46)	0.86 (1.45)	5.51
Comorbidities at baseline, n (%)			
Anxiety	190 (20.61)	187 (20.28)	0.81
Chronic pain	203 (22.02)	199 (21.58)	1.05
Depression	187 (20.28)	170 (18.44)	4.67
Osteoarthritis	470 (50.98)	466 (50.54)	0.87
Smoking	167 (18.11)	164 (17.79)	0.85
Cancer	132 (14.32)	116 (12.58)	5.09
Obesity	212 (22.99)	204 (22.13)	2.08
Substance use disorder	44 (4.77)	47 (5.10)	-1.50
Prior opioid exposure, n (%)[a]	349 (49.02)	344 (48.73)	0.58
Procedure year, n (%)[b]			
2019	204 (22.13)	263 (28.52)	-14.76
2020	225 (24.40)	228 (24.73)	-0.76
2021	232 (25.16)	228 (24.73)	1.03
2022	261 (28.31)	203 (22.02)	14.54

CCI, Charlson Comorbidity Index; LB, liposomal bupivacaine; PS, propensity score; SD, standard deviation; SMD, standardized mean difference. [a]Pharmacy (Part D) cohort. [b]Sensitivity analysis showed no influence on outcomes (medical cost, morphine milligram equivalents).

CUMULATIVE OPIOID PRESCRIPTIONS, DURATION OF USE, AND ORAEs

- LB use was marginally associated with fewer (~10%) MMEs (331 vs 361 MMEs; rate ratio [RR], 0.91 [95% confidence interval (CI)], 0.83, 1.01]; *P*=0.066) over 30 days after surgery versus non-LB use in the study cohort (Figure 2A)
  - Among patients with prior opioid exposure, those in the LB group were prescribed significantly fewer opioids versus those in the non-LB group (500 vs 576 MMEs; RR, 0.87 [95% CI, 0.77, 0.98]; *P*=0.022)

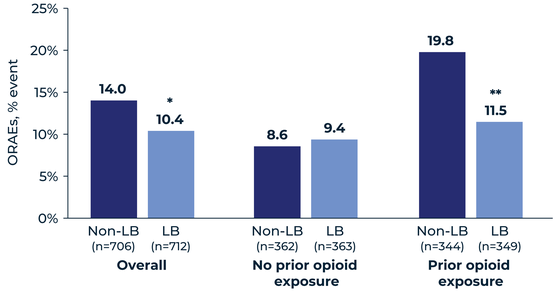
Figure 2. (A) Cumulative opioid prescriptions (in MMEs) and (B) opioid-treated days at 30-day follow-up in the LB and non-LB groups.



LB, liposomal bupivacaine; MME, morphine miligram equivalent. *P* values are for the rate ratio (not shown). *$P<0.05$. **$P<0.0001$.

- In addition, LB use was significantly associated with fewer (10%) opioid-treated days (6.5 vs 7.2 d; RR, 0.90 [95% CI, 0.86, 0.94]; *P*<0.0001) in the study cohort, and this difference was more pronounced (17%) among patients with prior opioid exposure (8.8 vs 10.6 d; RR, 0.83 [95% CI, 0.79, 0.87]; *P*<0.0001) (Figure 2B)
- LB use was also associated with a 26% lower rate of ORAEs (10.4% vs 14.0%; odds ratio, 0.71 [95% CI, 0.52, 0.98]; *P*=0.037) versus non-LB use (Figure 3)
  - A greater difference between groups was observed among patients with prior opioid exposure, with LB use showing a 42% lower rate of ORAEs (11.5% vs 19.8%; odds ratio, 0.52 [95% CI, 0.34, 0.80]; *P*=0.003) versus non-LB use

Figure 3. Percentage of opioid-related adverse events at 30-day follow-up in the LB and non-LB groups.

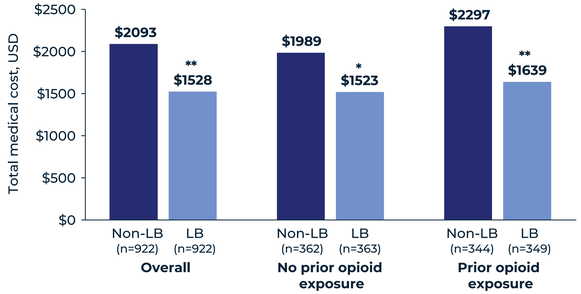


LB, liposomal bupivacaine; ORAE, opioid-related adverse event. *P* values are for the odds ratio (not shown). *$P<0.05$. **$P<0.01$.

MEDICAL COSTS

- Index surgery costs for the LB and non-LB groups were $8145 and $8120, respectively
- LB use was associated with 27% ($565) lower total medical cost at 30 days after surgery ($1528 vs $2093; RR, 0.73 [95% CI, 0.66, 0.81]; *P*<0.0001) versus non-LB use (Figure 4)
  - Similar reductions in total medical costs with LB use occurred in both those with and without prior opioid exposure (29% [$658] and 23% [$466] reductions, respectively; *P*<0.01 for both)

Figure 4. Total medical cost at 30-day follow-up in the LB and non-LB groups.



LB, liposomal bupivacaine; USD, United States Dollars. *P* values are for the rate ratio (not shown). *$P<0.01$. **$P<0.0001$.

- Cost savings with LB for the overall cohort were primarily attributable to inpatient costs (*P*=0.01) followed by emergency department costs (*P*=0.03)