



Combinatorial pharmacogenetic opioid-risk algorithms offer improved accuracy and reliability in predicting long term pain and opioid-related outcomes after lumbar spine surgery in adults

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INTRODUCTION

- Multilevel lumbar spinal fusion and decompression surgeries often require opioids in the postoperative period, despite their association with significant adverse effects ^[1].
- Long term out comes include chronic post-surgical pain (CPSP), opioid dependence and long-term opioid use ^[2].
- Postsurgical pain and opioid-related outcomes can vary considerably between patients.
- A combination of multiple genetic and clinical risk factors may provide a more reliable means of predicting long-term postoperative pain and adverse outcomes.

AIM

- The aim of this prospective, longitudinal study is to develop and validate combinational machine learning models to accurately identify patients at risk of opioid-related adverse outcomes mentioned above.

METHODS

- 205 adults undergoing lumbar spine surgery were enrolled.
- Patient demographics, clinical data, genetics, phenotype expression, and opioid usage were collected perioperatively and at one, three, and 12 months follow up.
- Machine learning classifiers (Lasso, Ridge, Elastic Net, SVM, XGBoost) were trained on 80% of the dataset.

RESULTS

- Models were selected using AUROC ceilings to mitigate overfitting, and optimal decision thresholds were determined using Youden's J-statistic.
- Final models were evaluated on a 20% holdout validation set (n = 41), with performance metrics (AUROC, sensitivity, specificity) bootstrapped to generate 95% confidence intervals.
- Validation models demonstrated strong performance in predicting long-term opioid-related adverse events.
 - The OUD model achieved an AUROC of 0.665, with sensitivity 0.5 and specificity 0.821.
 - The chronic post surgical pain model achieved an AUROC of 0.679, with balanced sensitivity 0.643 and specificity (0.650).
 - The model reflecting persistent postoperative opioid use at 1 month, achieved an AUROC of 0.861, with sensitivity 0.643, and specificity of 0.857 over highlighting its utility in identifying patients at risk for opioid consumption following discharge.

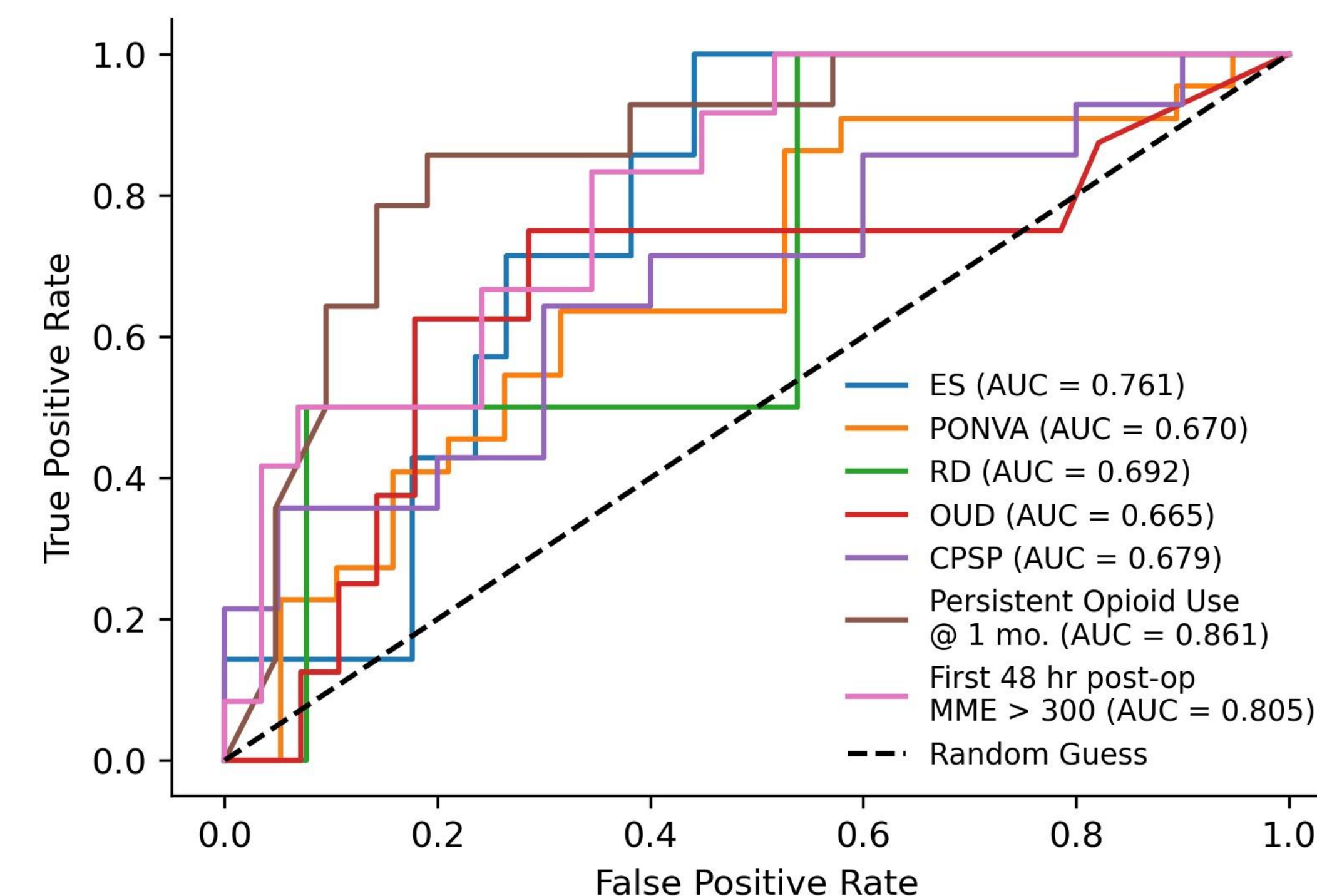


Figure 1. AUROC and Postoperative Outcomes. The highest discriminative ability is seen for Persistent Opioid Use at 1 month (AUC = 0.861), Moderate predictive performance is demonstrated for chronic postsurgical pain (CPSP) and opioid use disorder (OUD), with AUCs ranging from 0.665 to 0.679

Postoperative Outcomes	Incidence Rate	AUROC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
OUD	19.32%	0.665 (0.467, 0.867)	0.5 (0.143, 0.875)	0.821 (0.680, 0.960)
CPSP	39.18%	0.679 (0.451, 0.756)	0.643 (0.364, 0.9)	0.650 (0.421, 0.857)
Persistent Postoperative Opioid Use at 1 month	37.6%	0.861 (0.592, 0.895)	0.643 (0.385, 0.889)	0.857 (0.684, 1.0)

Table 1. Robust Combinatorial Prediction and Validation of Postoperative Opioid and Pain Outcomes. OUD = Opioid use disorder. CPSP = Chronic Postsurgical Pain. Persistent postoperative opioid use at 1 month achieves the highest performance, with an AUC of 0.861, strong specificity (0.857), and moderate sensitivity (0.643), suggesting it is the most accurate model in distinguishing high-risk individuals

DISCUSSION

- This study demonstrates that pharmacogenetic–clinical machine-learning models can effectively predict long-term opioid-related adverse events, providing robust algorithms for risk stratification.
- Such algorithms could enable early identification of at-risk patients and proactively mitigate serious opioid-related complications as well enhance surgical pain relief.
- Larger cohorts are warranted to refine these models and enable clinical translation.

REFERENCES

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