Identifying Risk Factors for Sialolithiasis

Karen Tawk, MD[1]; Abigail Dichter, BA[1]; Timothy Park, BA[1];
Mehdi Abouzari, MD, PhD[1]; Sepehr Oliaei, MD[1]

[1]Department of Otolaryngology, University of California, Irvine

Introduction

- Sialolithiasis is the leading cause of obstructive sialadenitis, with most stones forming in Wharton's duct.
- It occurs more often in men in their fifth to eighth decades and is uncommon in children except for a peak around age 10; patients typically present with periprandial pain and gland swelling.
- Ultrasound is the first-line imaging modality (high sensitivity for stones >2 mm, no radiation), and management ranges from conservative measures to transoral/endoscopic retrieval or laser lithotripsy to preserve gland function.
- Despite therapeutic advances, the pathogenesis and modifiable risk factors remain incompletely defined, including the roles of lifestyle, diet, medications, systemic conditions, and salivary stasis.
- This study employs machine-learning methods to identify potential risk factors for sialolithiasis, aiming to inform prevention, early diagnosis, and personalized treatment.

Methods

- A retrospective case-control study was conducted using the All of Us Research Program database (1980-2022).
- A total of 540 individuals diagnosed with sialolithiasis were identified and matched to controls by age, race, and gender, yielding 1080 participants in total.
- Data were collected on multiple variables, including acute tonsillitis, alcohol abuse, diabetes mellitus, kidney stones, cholelithiasis, gout, Sjögren's syndrome, hyperparathyroidism, smoking status, and others.
- Logistic regression analysis was performed using Python's Scikit-learn, with an L1-regularized model (α=0.001). Data were split into 70% training and 30% testing subsets.
- Model performance was evaluated using accuracy, sensitivity, specificity, F1 score, and ROC-AUC.
- Feature importance was determined by odds ratios and p-values (significance set at $p<0.05$).
- A complementary SHAP explainer analysis with XGBoost was used to assess the contribution of individual features to sialolithiasis risk at both the population and individual level.

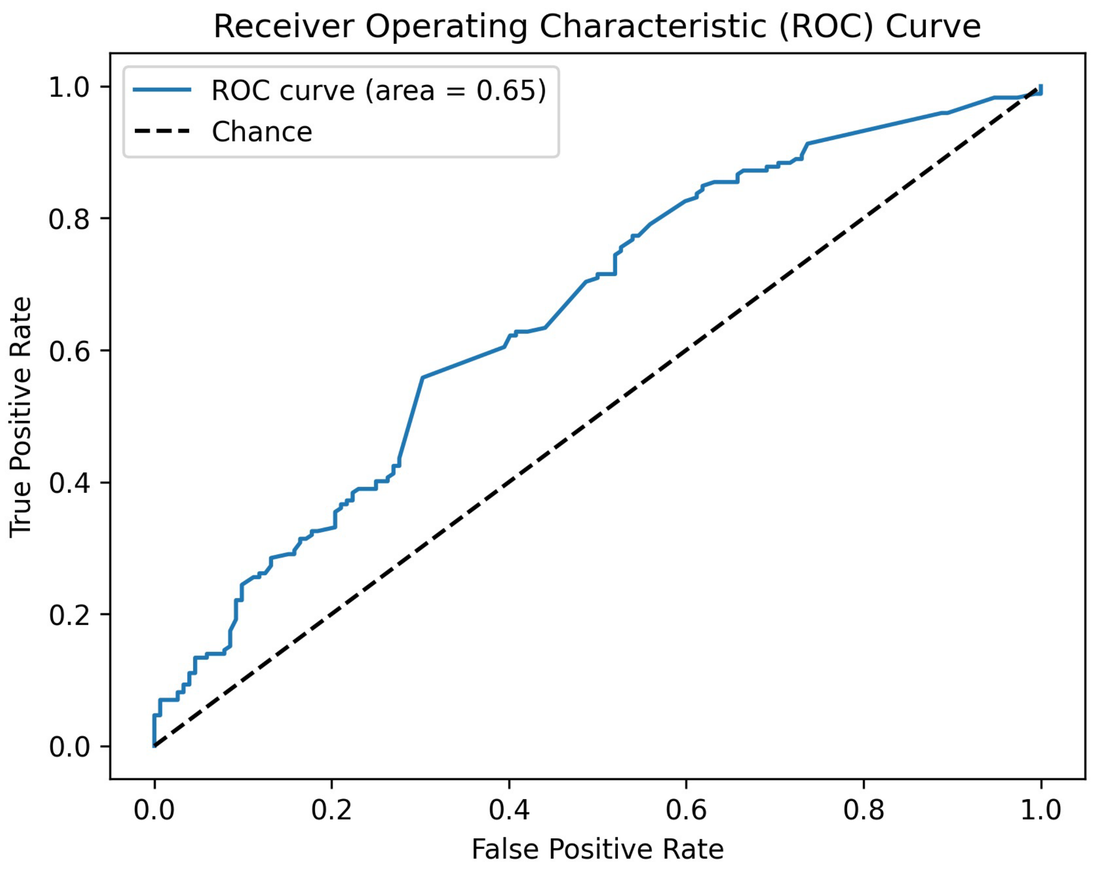

Figure 1. Receiver operating characteristic (ROC) curve for the multivariate logistic regression model predicting sialolithiasis (AUC = 0.65), indicating modest discriminative performance.

Table 1. Adjusted Odds Ratios for the Association Between Comorbid Conditions and Sialolithiasis

Covariates	OR (95% CI)	*p*-value
Cholelithiasis without obstruction	2.14 (1.24-3.72)	**0.007***
Obesity	1.72 (1.32-2.25)	**<0.001***
Hyperparathyroidism	1.57 (0.76-3.24)	0.222
Osteoporosis	1.46 (1.04-2.05)	**0.029***
Dehydration	1.41 (0.96-2.06)	0.077
Acute tonsillitis	1.35 (0.56-3.26)	0.510
Hypercalcemia	1.33 (0.76-2.31)	0.314
Sjögren's syndrome	1.26 (1.04-2.05)	0.49
Alcohol abuse	1.21 (0.78-1.90)	0.412
Systemic lupus erythematosus	1.08 (0.53-2.19)	0.83
Smoking	1.06 (0.73-1.53)	0.765
Type II diabetes mellitus without complication	0.94 (0.71-1.24)	0.659
Gout	0.92 (0.59-1.45)	0.728
Bipolar disorder	0.87 (0.53-1.42)	0.58
Kidney stone	0.85 (0.58-1.24)	0.396
Gallstone	0.79 (0.44-1.40)	0.421
Essential hypertension	0.58 (0.47-0.72)	**<0.001***

*Statistically significant p-value

Results

- Among the 1,080 participants analyzed (mean age 66.8 ±14.1 years), 540 (50%) had a diagnosis of sialolithiasis.
- Cholelithiasis without obstruction was strongly associated with sialolithiasis (OR=2.14, 95% CI: 1.23-3.72, p=0.007).
- Obesity (OR=1.72, 95% CI: 1.32-2.25, p<0.001) and osteoporosis (OR=1.46, 95% CI: 1.04-2.05, p=0.029) were also significant predictors.
- Essential hypertension was negatively associated with sialolithiasis, suggesting a potential protective effect (OR=0.58, 95% CI: 0.47-0.72, p<0.001).
- Dehydration trended toward significance (OR=1.41, 95% CI: 0.96-2.06, p=0.077), while other comorbidities were not significant (**Table 1**).
- The logistic regression model achieved ROC-AUC=0.653, accuracy=57.1%, sensitivity=44%, and specificity=53%.
- SHAP analysis identified essential hypertension (SHAP=0.345), obesity (0.325), type 2 diabetes (0.198), and dehydration (0.176) as the most influential features.
- Additional contributors included cholelithiasis without obstruction (0.139), alcohol abuse (0.126), osteoporosis (0.124), and smoking (0.112).

Conclusions

- Cholelithiasis, obesity, and osteoporosis were significant predictors of sialolithiasis, while hypertension showed an inverse association, suggesting systemic metabolic links beyond local duct pathology.
- Conflicting evidence across studies underscores the multifactorial nature of sialolithiasis, likely involving metabolic, inflammatory, and pharmacologic factors.
- Broader risk assessment and prospective studies are needed to clarify causal pathways and guide personalized prevention and management.

Contact

Mehdi Abouzari, MD, PhD & Sepehr Oliaei, MD
Department of Otolaryngology–Head and Neck Surgery, University of California, Irvine
333 City Blvd West, Suite 525, Orange, CA, 92868
Phone: (714) 456-5753
Fax: (714) 456-5747
Emails: mabouzar@hs.uci.edu & soliaei@hs.uci.edu

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