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Development and validation of an AI model predicting post-extraction complications: A multicenter cohort study protocol

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Dry socket (alveolar osteitis) and post-operative surgical-site infection (SSI) are most common complications affecting 1-20% extraction sites. Risk factors include smoking, diabetes, prolonged surgery and operative trauma. A multicenter cohort using retrospective derivation ($n \approx 2000$, 3–5 centers) and prospective validation (12–18 months, ≥ 2 centers) will be done. The patients included will be adults ≥ 18 years undergoing extraction and outcome assessed will be dry socket (pain, exposed bone days 1–5); SSI (purulence/swelling within 30 days). The expected outcome model should be able to predict the prognosis of the dry socket and SSI, thus reducing the injudicious use of antibiotics and increase in expertise of the surgeon.

Keywords: Dry socket, surgical site infection, machine learning, tooth extraction, comorbidities**Background:**

Dry socket, or alveolar osteitis, is highly painful complications observed after tooth extractions caused due to partial or complete disintegration/loss of intra-alveolar blood clot. This results in exposure of alveolar bone and associated halitosis [1]. The incidence ranges from 1-2% in uncomplicated extractions to as high as 20–30% in cases of impacted teeth, traumatic surgical technique or predisposing patient factors. [2] Another common complication is post-operative surgical-site infections (SSIs), affecting approximately 1-13% of extractions, symptoms may present as purulent discharge, localized cellulitis, or abscess formation requiring systemic antimicrobial therapy, incision and drainage [3]. Dry socket and SSI have been extensively studied and documented along with their multifactorial etiology. The meta-analyses and systematic review include various patient related risk factors too. This included include current tobacco smoking (pooled odds ratio (OR) 3.8 across meta-analyses), systemic steroid use, diabetes mellitus, systemic complications and immunosuppressive disorders. These affects wound healing, clot stability and host defense [4, 5]. The procedure-related risk of these two complications is equally accountable, this includes: prolonged operative time extensive bone removal, intraoperative root fracture and less experience of operator. In prospective cohort study, these determinants have been associated with increased complication rate [6]. In a landmark electronic dental record data-mining study of thousands of extractions further showed that documented histories of serious systemic illness (OR 1.4), malignancy (OR 2.6) and recurrent oral ulceration (OR 1.9) significantly increased the odds of dry socket, underscoring the predictive value of comorbidity profiles

captured in routine clinical documentation [7]. There has been evidence base which remains qualitative and dependent on clinical judgment but risk stratification for dry socket and SSI and a standardized, validated prediction tools remains elusive. Artificial intelligence (AI) and machine learning (ML) can substantially advance post-operative risk prediction [8]. Across 24 studies, a recent systematic review evaluated 85 machine learning models for predicting surgical site infections and found that externally validated models achieved a median C-statistic of 0.79 [8]. Comorbidities such as diabetes (included in 75% of models), systemic corticosteroid use (85%) and smoking (80%) were incorporated as predictors in the vast majority of models, making them nearly universal risk factors [9]. Tree-based ensemble approaches, including random forests and gradient boosting methods, often outperformed traditional logistic regression, particularly when modeling nonlinear patterns and higher-order interactions between patient-level and procedure-level variables [10]. In oral surgery, AI applications have not been explored in to their full potential except for pre-operative imaging (*e.g.*, cone-beam computed tomography for alveolar bone loss or impaction classification); prediction of extraction difficulty and estimation of inferior alveolar nerve injury risk have been considered. However, post-operative healing complications such as dry socket or SSI [11, 12] are largely neglected for LLM. In a recent systematic review of AI in tooth extraction had confirmed this where there was no identified model which was specifically designed to predict post-operative infections or fibrinolytic endpoints despite their predictive presence [13]. Therefore, it is of interest to report and explore the potential role of large language models and machine learning–

based predictive systems in identifying patients at increased risk of post-operative complications such as dry socket and surgical-site infections following tooth extraction, particularly through the integration of systemic comorbidities, behavioral risk factors and procedure-related variables into standardized risk prediction frameworks.

Materials and Methods:

This multicenter cohort study employed a two-phase hybrid design to maximize generalizability. Phase 1 comprised a retrospective derivation cohort assembled from electronic dental records (EDRs), operative logs and post-operative clinic records collected over the preceding 5–10 years across participating dental institutions and clinics. Phase 2 consisted of a prospective external-validation cohort enrolling consecutive eligible patients indicated for extraction over 12–18 months at a minimum of two participating centers. This approach allowed the model's performance to be examined across both time and different clinical settings. By drawing on large datasets to secure an adequate number of outcome events, while simultaneously testing performance in up-to-date routine practice, the study balanced statistical power with contemporary real-world validity. The study protocol received institutional review board approval at all participating sites and was conducted in accordance with the Declaration of Helsinki. Retrospective data use proceeded under waiver or exemption of individual informed consent where permitted by local regulations, while prospective participants provided written informed consent prior to enrollment. Inclusion criteria encompassed adults aged ≥ 18 years undergoing elective tooth extraction or minor dentoalveolar surgical procedures, including simple forceps extractions and surgical extractions with flap elevation and/or ostectomy such as impacted mandibular third-molar removal, performed under local anesthesia, intravenous sedation, or general anesthesia. Eligible cases required complete perioperative documentation, including pre-operative medical history, intraoperative timing and technique details and a minimum follow-up period of 7–14 days for outcome ascertainment. Exclusion criteria removed cases whose complication risk profiles substantially diverged from routine ambulatory oral surgery practice, including extractions performed as part of major oncologic resection, orthognathic surgery, or maxillofacial trauma reconstruction, patients lost to follow-up before the predefined outcome window and records with irretrievable missingness in core predictor variables such as smoking status or surgical duration. Two co-primary binary outcomes were modeled separately to enable precise risk communication and targeted preventive strategies. Dry socket (alveolar osteitis) was defined as new-onset or worsening severe pain at or around the extraction site within postoperative days 1–5, accompanied by clinical evidence of partial or complete loss of the intra-alveolar blood clot with exposed alveolar bone, with or without fetor oris and excluding cases with frank suppuration meeting SSI criteria. Post-extraction surgical-site infection (SSI) was defined as clinical diagnosis of localized purulent discharge, abscess formation, or pronounced erythema or induration at the

extraction site necessitating unplanned systemic antimicrobial therapy, incision and drainage, or other re-intervention within 30 post-operative days. Outcomes were systematically ascertained using structured EDR fields, such as ICD-10 complication codes and prescriptions for rescue antibiotics, supplemented by natural language processing of free-text clinical notes and manual adjudication by blinded oral and maxillofacial surgeons for ambiguous cases. A pre-specified set of 18 candidate predictors was selected to balance comprehensiveness and parsimony, informed by prior literature and clinical plausibility to optimize the signal-to-noise ratio [8, 16–18]. Pre-operative variables included age, sex, body mass index (kg/m^2), smoking status, associated comorbidities and addictions such as alcohol or tobacco use. Comorbidities included diabetes mellitus, cardiovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, active malignancy, autoimmune disease, immunosuppressive conditions and prior head and neck radiotherapy. Medications affecting bone healing and metabolism, including corticosteroids, bisphosphonates, antiplatelet and anticoagulant agents and chronic immunosuppressive therapies, were also considered. Operator- and tooth-level predictors included surgical duration in minutes from incision to final suture placement or socket closure, tooth-specific characteristics such as mandibular third molar versus other teeth, impaction type according to Pell-Gregory and Winter classifications, radiographic difficulty score, technical variables including flap type and amount of bone guttering or ostectomy, operator experience level and intraoperative adverse events such as root fracture, excessive blood loss and proximity to neural structures. The anticipated incidence of dry socket was approximately 10% (range 6–22% in mandibular third-molar extraction cohorts), with SSI rates of 3–6%. The derivation cohort was therefore powered to yield a minimum of 200 events per primary endpoint, enabling estimation of 15–20 effective model parameters in accordance with updated recommendations for clinical prediction model development emphasizing event-per-variable thresholds of ≥ 15 . This minimized overfitting and supported robust internal validation through shrinkage correction. Approximately 2000 retrospective and prospective extraction cases were therefore required through multicenter data collection. With an anticipated shrinkage of 0.10–0.15, simulation-based power calculations reduced bias related to model shrinkage and provided adequate precision for discrimination metrics with 95% confidence intervals and area under the curve (AUC) estimates ≤ 0.10 . The external validation process enrolled at least 100 events per parameter to ensure reliable model transportability and calibration. Data from all centers were entered into a centralized database using standardized definitions. For missing predictor data up to 20%, multiple imputations by chained equations were used under the assumption that data were missing at random. Outcome and auxiliary variables were incorporated into the imputation models and sensitivity analyses further evaluated the effect of missing data. Continuous predictors were assessed for nonlinearity using fractional polynomials or spline

transformations, while implausible outliers prompted source verification to minimize bias. Separate prediction models were developed for dry socket and SSI. The baseline approach utilized logistic regression analysis, with the regularization parameter λ selected through cross-validation to promote sparsity, reduce overfitting and maintain predictor stability. Forest plots were used for comparison and interpretation, while XGBoost models with early stopping and a learning rate of 0.1 were implemented to address complex interactions and non-linear patterns in surgical outcome prediction. Model evaluation incorporated several performance metrics at each stage. Discrimination was assessed using the DeLong method for AUC estimation with 95% confidence intervals. Calibration was evaluated using calibration intercepts and slopes, Hosmer-Lemeshow testing, calibration plots and Brier scores, while overall fit was examined using Nagelkerke R^2 . Clinical usefulness was assessed through decision-curve analysis across realistic risk thresholds of 5–30%, comparing the models against “treat-all” and “treat-none” strategies. External validation involved direct application of the finalized models to the prospective validation cohort without refitting. If significant calibration drift was observed, such as calibration intercepts >0.2 , recalibration methods including Platt scaling were considered. Model interpretability was enhanced using permutation importance methods, partial dependence plots and SHAP values to assess how comorbidities interacted with surgical duration and other factors in increasing the incidence of dry socket and SSI. Ultimately, the model outputs were simplified into a three-tier risk stratification system (low, moderate and high risk) accompanied by a web-based calculator for integration into electronic dental records. Statistical analyses were conducted using R (v4.4) and/or Python packages including scikit-learn, XGBoost and SHAP. Following necessary approvals, anonymized datasets and source code were deposited into public repositories to support transparency and reproducibility.

Results:

The study is expected to enroll approximately 2,000 cases across the retrospective derivation and prospective validation cohorts, with approximately 1,400 cases in the derivation cohort and 600 cases in the validation cohort. The derivation cohort is expected to provide adequate statistical power for evaluating 18 candidate predictors, with more than 200 events anticipated for each primary endpoint. The anticipated baseline characteristics and prevalence of major comorbidities are presented in **Table 1**. Smoking is expected in approximately 22% of the derivation cohort and 21% of the validation cohort, while diabetes mellitus is anticipated in 12% and 11%, respectively. Surgical procedures lasting more than 30 minutes are expected in approximately 18% and 19% of the respective cohorts. The anticipated incidence of dry socket is approximately 10% in the derivation cohort and 9.8% in the validation cohort, while the incidence of surgical site infection (SSI) is expected to be approximately 4% in both cohorts. The XGBoost models are anticipated to demonstrate good discrimination for both primary outcomes and to

outperform traditional logistic regression, particularly in capturing nonlinear relationships and interactions among clinical predictors. As shown in **Table 2**, the anticipated AUC-ROC for dry socket is 0.79–0.85 in the derivation cohort and 0.74–0.82 in the validation cohort, with corresponding Brier scores of 0.082 and 0.091. For SSI, the anticipated AUC-ROC is 0.80–0.88 in the derivation cohort and 0.72–0.82 in the validation cohort, with Brier scores of 0.035 and 0.042, respectively.

Table 1: Baseline characteristics and prevalence of comorbidities

Variable	Derivation Cohort (n≈1400)	Validation Cohort (n≈600)
Smokers	22%	21%
Diabetes Mellitus	12%	11%
Surgical Duration (>30 min)	18%	19%
Incidence of Dry Socket	10%	9.80%
Incidence of SSI	4%	4%

Table 2: Predictive performance metrics (primary endpoints)

Outcome	Metric	Derivation - 95%CI	External Validation - 95%CI
Dry socket	AUC-ROC	0.79-0.85	0.74-0.82
	Brier score	0.082	0.091
SSI	AUC-ROC	0.80-0.88	0.72-0.82
	Brier score	0.035	0.042

Discussion:

This protocol is an attempt to develop first AI-based clinical prediction model using comprehensive framework targeting dry socket and post-extraction SSI. There will be an explicit emphasis on the all the precursor which lead to this complication including patient comorbidities and surgical duration using an imaging-centric AI applications [14]. This consolidation of risk factors of comorbidities such as smoking, diabetes, immunosuppression, prolonged surgical time will produce a unified, data-driven modeling strategy. This will lead to specialty-specific, externally validated prediction models [15]. The anticipated performance targets (AUC ≥ 0.80 in derivation and ≥ 0.75 in external validation) are consistent with existing models for third-molar complications [16] and benchmarked performance for externally validated SSI prediction models in general surgery studies [17]. This will offer the potential to support risk stratified interventions including targeted antibiotic administration and post-operative care. The methodology includes the multicenter design which reduces the single center bias which is strength of the study. The entire data collection and reporting will be done as per TRIPOD+AI guidance keeping everything transparent including missing data, fine tuning of then models and performance evaluation [18]. Along with it, parallel development complex tree-based models to remove inter operative reliability and ensure predictive accuracy. The model includes pre-specified explainability analyses to assess for relative influence of comorbidities on procedural factors. The retrospective–prospective design balances for any rare event occurrence and at the same time considering the contemporary routine practice being most relevant. There are certain limitations to this protocol which includes possible heterogeneity in EDR structure will require substantial coding to harmonize data. Confounders such as patients’ attitude and practice including adhering to post-operative instructions and

use of mouthwash needs to be addressed. Generalizability beyond academic centers will require dedicated transportability studies. Nonetheless, if the study could be translated into clinical workflows, the prediction tools will be of great importance to oral surgery practice. Preventive strategies to minimize the risk factors could be efficiently applied to reduce the incidence of dry socket and SSI.

Conclusion:

This multicenter cohort study aims to develop and validate an explainable AI model for predicting dry socket and surgical site infection after dental extraction. The model will integrate patient comorbidities with key procedural factors to enable individualized post-operative risk stratification. Its clinical application may support targeted prevention, reduce unnecessary antimicrobial use and improve post-operative care.

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