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## Review article

# Artificial intelligence applications in the diagnosis and management of cleft lip and palate: An updated review

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anomalies

**Abstract** According to the U.S. National Institutes of Health, cleft lip and/or palate (CL/P) is one of the most common congenital anomalies, significantly affecting both function and aesthetics while placing a considerable burden on healthcare systems worldwide. With the rapid advancement of artificial intelligence (AI) in various medical fields, a thorough evaluation of its role in CL/P management has become essential. Therefore, this review was undertaken to summarize recent clinical applications of AI in the diagnosis, treatment, and care of CL/P. A comprehensive search of PubMed and IEEE Xplore was conducted from January 1, 2015, to May 31, 2025, using combined keywords related to AI and CL/P. Of the 134 records initially identified, 51 full-text articles met the eligibility criteria and were included in the final analysis. In conclusion, AI is driving innovation in CL/P management across multiple domains; however, further evidence from diverse populations and the establishment of clear ethical frameworks are required to ensure its long-term clinical applicability.

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## Introduction

Cleft lip and/or palate (CL/P) is one of the most common craniofacial anomalies, resulting from complex interactions between genetic and environmental factors.<sup>1</sup> These defects primarily arise during embryonic development, when the medial nasal process fails to establish or maintain contact with the lateral nasal and maxillary processes.<sup>2</sup> CL/P may involve the lip, the hard palate, and can extend to the soft palate. In some cases, the cleft also affects adjacent soft tissue structures of the face, leading to more complex orofacial clefts.<sup>3</sup>

The prevalence of CL/P varies according to race, geography, socioeconomic status, and cleft type. A systematic review conducted by Salari et al. estimated the global prevalence of orofacial clefts.<sup>4</sup> The prevalence of lip cleft was reported as 0.30 per 1000 live births based on 57 reviews including 17,907,569 participants. Palate cleft had a prevalence of 0.33 per 1000 live births from 59 reviews comprising 21,088,517 participants, whereas cleft lip and palate combined showed the highest prevalence at 0.45 per 1000 live births, derived from 55 reviews including 17,894,673 participants. Among global populations, studies consistently report the highest occurrence in Asians, followed by Caucasians, with the lowest incidence observed in individuals of African descent.<sup>5–7</sup> In China, a meta-analysis covering the period 1986–2015 reported an overall incidence of orofacial clefts as high as 1.4 per 1000 live births.<sup>8</sup> In the United States, cleft lip with or without cleft palate ranks as the fourth most common congenital anomaly.<sup>3</sup> Recent US national data (2016–2020) report prevalence rates of 0.34 per 1000 for cleft lip, 0.62 per 1000 for cleft palate, and 0.65 per 1000 for combined cleft lip and palate, which are slightly higher than the global estimates reported above.<sup>9</sup> Regarding socioeconomic status, family income has been identified as a potential determinant of cleft prevalence.<sup>10</sup> Sabbagh et al. reported that lower monthly family income was associated with a higher occurrence of orofacial clefts, whereas higher income was linked to a reduced prevalence.<sup>11</sup> CL/P significantly impacts quality of life and imposes substantial treatment costs on both families and healthcare systems. Beyond the aesthetic consequences, infants with CL/P frequently experience feeding difficulties that may impair physical growth. If left untreated, CL/P can severely affect speech development and, in some cases, lead to hearing loss or malocclusion.<sup>12</sup> According to the U.S. National Institute of Dental and Craniofacial Research, healthcare costs for children aged 1–10 years with combined cleft lip and palate are six times higher than those for unaffected children.<sup>13</sup> Consequently, comprehensive management presents particular challenges, especially in developing countries.

Given the morphological diversity of CL/P, its diagnosis and treatment require a multidisciplinary approach tailored to the needs of each patient. Advances in molecular

biomedicine now provide counseling resources for couples prior to conception.<sup>14</sup> Prenatally, CL/P can often be detected through multiplanar ultrasound performed by obstetricians.<sup>15</sup> Before surgery, orthodontists may employ non-invasive appliances such as nasoalveolar molding to reduce craniofacial discrepancies.<sup>16</sup> By approximately three months of age, reconstructive surgery is typically performed, aiming not only to restore biological function but also to improve facial aesthetics.<sup>17</sup> Nevertheless, many patients continue to experience speech impairments, making early speech-language therapy essential.<sup>18</sup> In addition, maxillary growth deficiency is frequently reported in CL/P patients and often results in skeletal Class III malocclusion.<sup>19,20</sup> In such cases, bone grafting and orthognathic surgery may be necessary to achieve stable functional and aesthetic outcomes.

One of the most impressive technological advances today is Artificial intelligence (AI). By processing large volumes of medical data with complex algorithms, AI systems can learn and improve performance across various scenarios.<sup>19</sup> With its growing potential, AI has been rapidly applied in medicine, including CL/P care. In this field, AI has demonstrated its value in multiple domains, including imaging diagnostics, intraoral assessment, reconstructive surgery, and speech therapy.<sup>15–17,20</sup> As its role in the multidisciplinary management of CL/P becomes increasingly evident and related advancements continue to emerge, this updated review was undertaken to summarize and synthesize the recent applications of AI in the diagnosis, treatment, and care of patients with CL/P.

## Materials and methods

### Information sources and search strategy

To address the question, “In what aspects can AI be applied to support the diagnosis, treatment, and care of patients with CLP?” we conducted a full-text review using relevant search terms across two databases: PubMed and IEEE. The following search string was entered into each database: (“cleft lip” OR “cleft palate” OR “cleft lip and palate” OR “orofacial clefts”) AND (“artificial intelligence” OR “machine learning” OR “deep learning” OR “neural networks” OR “convolutional neural network”).

### Selection criteria

The search was restricted to articles published between January 1, 2015, and May 31, 2025, to capture recent applications of AI. Inclusion criteria were studies directly related to the application of AI, machine learning (ML), or deep learning (DL) in the diagnosis, treatment, or care of CL/P. Eligible study designs included observational studies,

model validation studies, and systematic or narrative reviews. Only articles published in English were considered. Exclusion criteria were abstracts without accessible full texts, non-scientific materials such as book chapters, editorials, announcements, letters, single case reports, or small case series.

### Article selection and data extraction

The search protocol was developed in accordance with the PRISMA 2020 framework for systematic reviews and followed a three-step process (Fig. 1). First, potentially relevant records were retrieved using predefined inclusion criteria and a comprehensive search string. Duplicate articles identified across databases were removed prior to screening.

In the second step, two independent reviewers carefully assessed the titles, abstracts, and full-text availability of the retrieved articles to determine eligibility. In cases of disagreement, a third reviewer evaluated the article and discussed it with the initial reviewers until a consensus was reached. Finally, all studies that met the inclusion criteria were analyzed in depth to determine which main aspects of CL/P diagnosis, treatment, or care were supported by AI, and to describe how AI was applied in these contexts.

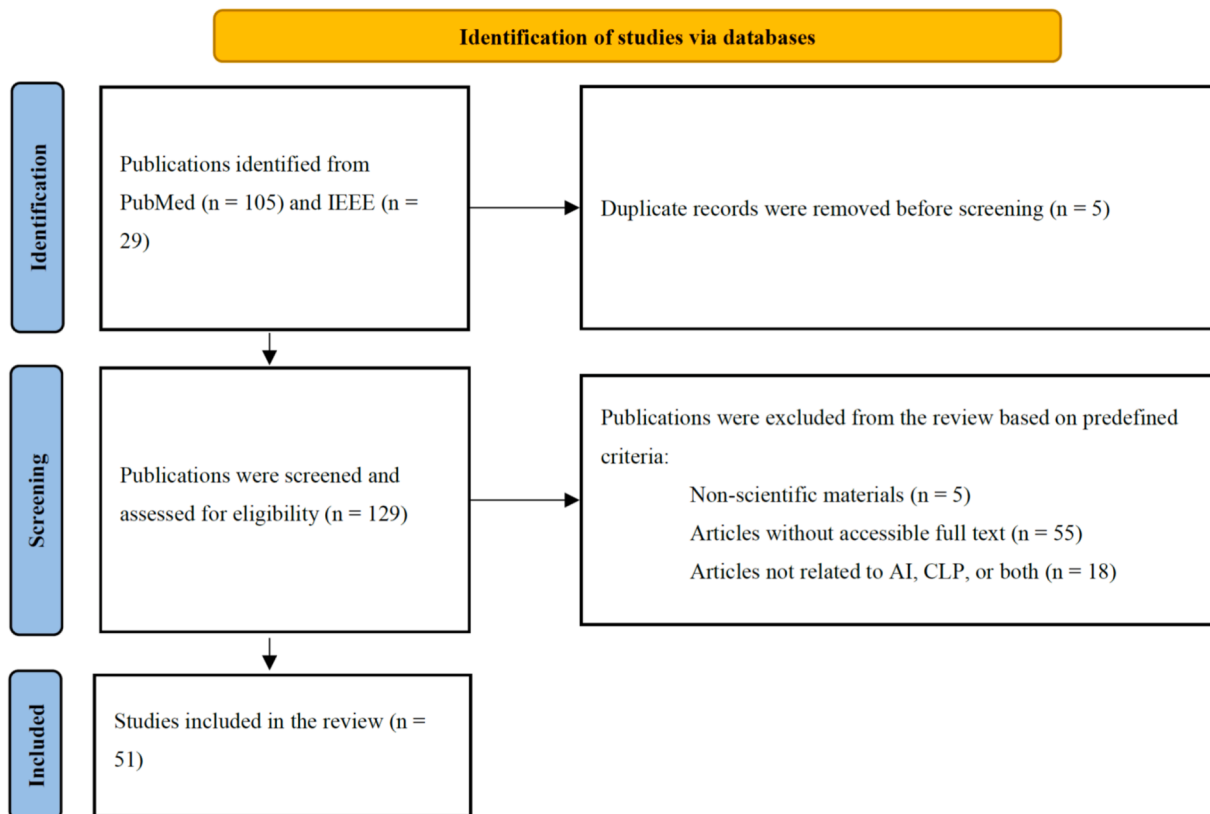
### Results

From the two databases, PubMed (n = 105) and IEEE (n = 29), a total of 134 records were initially identified. After

the removal of five duplicates, 129 records remained for title and abstract screening. During the eligibility assessment, 78 studies were excluded for the following reasons: non-scientific materials (n = 5), inaccessible full texts (n = 55), and studies not related to AI, CL/P, or both (n = 18). Ultimately, 51 full-text articles that met all inclusion criteria were included in the detailed review. To provide a clearer overview of their scope, these studies were further analyzed and categorized into seven main groups based on their primary applications. Imaging diagnosis accounted for the largest number, with 13 studies,<sup>15,21–32</sup> followed by speech-language therapy (n = 8),<sup>18,20,33–38</sup> genetic and molecular approaches (n = 8),<sup>14,39–45</sup> surgical intervention (n = 6),<sup>17,46–50</sup> intraoral diagnosis (n = 6),<sup>16,51–55</sup> risk prediction (n = 2),<sup>56,57</sup> and caregiver education (n = 3).<sup>58–60</sup> In addition, five review articles provided a broader perspective by addressing multiple aspects of AI applications in CL/P.<sup>19,61–64</sup>

### Imaging diagnosis

Multiplanar ultrasound during mid-gestation remains one of the most reliable and accurate methods for evaluating CL/P. However, it has certain limitations, including lengthy examination times and dependence on operator expertise. To address these drawbacks, He developed CLP-Net, a model that automatically identifies diagnostic planes on 3D ultrasound images.<sup>15</sup> This system received highly positive feedback from experts and reduced examination time by



**Figure 1** Flow diagram of study selection based on the PRISMA 2020 guidelines. AI: artificial intelligence; CL/P: cleft lip and/or palate.

15 s (31.3 %) for experienced clinicians and by 63 s (38.9 %) for less experienced practitioners. Another challenge in applying ML to CL/P ultrasound diagnosis is the limited availability of high-quality imaging data, which is often difficult to collect due to ethical concerns. To overcome this, Nantha et al. proposed a few-shot learning framework that integrates Vision Transformers with Siamese Neural Networks (SNNs), combining ultrasound tongue images with speech spectrograms.<sup>22</sup> By leveraging multimodal features from both imaging and speech data, the model achieved 82.76 % classification accuracy across three CL/P subtypes and demonstrated potential for application in data-limited settings.

In the diagnosis of CL/P using 2D panoramic radiographs, Kuwada et al. introduced two DL models built on the DetectNet architecture.<sup>26</sup> Model 1 was trained on unilateral alveolar cleft (AC) cases, while Model 2 included both AC patients and healthy controls. Model 2 demonstrated lower false-positive rates and higher overall accuracy compared with both Model 1 and human observers. To further differentiate between unilateral and bilateral AC, the authors extended their work by developing four additional models: Model U (unilateral AC + controls), Model B (bilateral AC + controls), Model C1 (unilateral + bilateral AC + controls), and Model C2 (similar to C1 but with expanded input features).<sup>27</sup> Diagnostic sensitivity improved across models, with Model C2 achieving the highest performance (0.89), comparable to that of experienced radiologists.

In subsequent work on palate clefts (PC), two models were proposed: Model A, which employed DetectNet to identify the maxillary incisor region before classifying PC, and Model B, which used VGG-16 to directly analyze panoramic images.<sup>25</sup> Model A achieved the best results with perfect sensitivity and specificity (AUC = 0.95), outperforming both Model B (AUC = 0.93) and radiologists (AUC = 0.70 and 0.63).

Early detection of anomalies such as missing, ectopic, or morphologically abnormal teeth is also crucial for CL/P treatment planning. Diagnocat, a convolutional neural network (CNN)-based software, was evaluated for tooth detection and classification in panoramic radiographs of CL/P patients.<sup>21</sup> The software demonstrated high sensitivity ( $0.98 \pm 0.03$ ) and precision ( $0.96 \pm 0.04$ ), although performance varied by age group and anatomical location, with younger patients and the left maxillary region showing higher rates of false-positive and false-negative results.

For cephalometric analysis, ML models have also been applied to automate landmark identification.<sup>28</sup> Alam and Alfawzan investigated dental characteristics in individuals with and without CL/P and found significant differences in eight dental variables.<sup>30</sup> Regarding craniofacial structures, individuals with CL/P exhibited significantly reduced SNA, ANB, and Wits appraisal values compared with the non-cleft group, whereas SNB showed no difference.<sup>31</sup> In addition, a higher prevalence of Sella Turcica bridging was observed in the CLP group.<sup>32</sup>

More recently, 3D imaging techniques have shown considerable promise in assessing cleft-related defects. Miranda et al. developed a DL model capable of classifying the severity of alveolar cleft defects reconstructed from CBCT images, achieving high accuracy (0.823) and

sensitivity (0.816).<sup>23</sup> Wang et al. applied a 3D U-Net to automatically segment the maxilla and cleft region on CBCT scans and identified significant hypoplasia of the maxilla on the cleft side, particularly in the pyriform aperture and alveolar crest regions adjacent to the defect.<sup>29</sup> Furthermore, 3D U-Net has been used to reconstruct and autofill cleft defects, providing clinicians with a predictive understanding of how alveolar bone grafting may influence maxillary development.<sup>24</sup>

## Intraoral diagnosis

In clinical practice, intraoral examination plays an important role in establishing treatment plans for children with CL/P. Traditional dental impressions with alginate are commonly used for defect analysis; however, this method has several drawbacks, including material deformation, patient discomfort, and difficulty in accurately capturing the dental arch morphology. The development of 3D scanning technology, combined with AI support, has provided promising alternatives. Smartphones have been employed as substitutes for professional scanners to generate 3D surface models of intraoral structures. For example, the KIRI Engine application was shown to produce 3D scans with minimal error (approximately 0.22 mm), comparable to specialized scanning devices.<sup>51</sup> Complementing this, Lingens et al. introduced a method leveraging CNN-supported landmark detection from single CL/P images to enable 3D reconstruction.<sup>54</sup> Although performance on real patient images was lower than that achieved with synthetic data, the findings suggest that expanding datasets could improve reliability. Collectively, these approaches offer strategies that overcome the limitations of traditional methods while remaining affordable in low-resource settings. In addition, Agaronyan et al. developed a DL model capable of automatically recognizing anatomical landmarks on 3D palatal models of CL/P infants, achieving 94.44 % accuracy with a mean absolute error of  $1.676 \pm 0.959$  mm.<sup>55</sup> Woodsend et al. also introduced an automated dental landmarking tool that demonstrated high applicability.<sup>53</sup> These AI-assisted 3D models provide a rapid and accurate means of designing preoperative orthopedic plates.<sup>52</sup> Schnabel et al. further emphasized that appliances fabricated with AI support achieved excellent fit (average error of about 0.1 mm) and rapid design times (less than 3 min).<sup>16</sup>

## Surgical intervention

Surgical repair of CL/P is often the most critical step in restoring the facial structure of affected children. Typically performed at around three months of age, the procedure aims not only to restore biological function but also to improve facial aesthetics.<sup>65</sup> Sayadi et al. developed a ML model based on High-Resolution Net that automatically recognized anatomical landmarks on CL/P patient images and videos with a mean error of 0.029–0.055, thereby supporting more precise determination of surgical incision lines.<sup>17</sup> In contrast to approaches that rely on anatomical landmarks, Rosero et al. proposed a DL model using a SNN to assess lip symmetry, an important aesthetic indicator

after surgery. This model employed a contrastive method to objectively compare both halves of the lip.<sup>41</sup>

Evaluating surgical outcomes plays a critical role in refining techniques and improving treatment quality. Recently, ML has been applied to simulate facial morphology and predict clinical results. Hayajneh et al. presented a technique based on StyleGAN2 model adaptation to assess the extent of facial deformity.<sup>49</sup> This method reconstructed a normalized version of the patient's face and measured the difference between the original and simulated images to calculate a deformity score, rather than relying solely on clinician evaluation. It provided an objective measurement of defects and demonstrated a strong correlation with expert assessments. However, a major limitation of StyleGAN models is their requirement for large training datasets, while real patient images are not always easily obtainable. Moreover, the potential for data leaks raises privacy concerns, as patient identities could be inadvertently revealed. To address these issues, Chen et al. proposed an inpainting model based on convolutional neural networks (CNNs) that reconstructs affected regions from patient images using only normal facial data for training, thereby ensuring data privacy.<sup>50</sup> Hayajneh et al. further improved the inpainting technique by incorporating discrepancy optimization.<sup>46</sup> This enhanced system reconstructed facial images, identified the location and severity of deformities, and demonstrated rapid processing times with strong correlation to expert opinions, making it a valuable tool for treatment planning and post-operative monitoring. In addition, Hayajneh et al. introduced CleftGAN, a model capable of generating synthetic cleft images to support ML training and validation.<sup>47</sup> The model produced facial images with cleft features derived from normal faces and improved realism by integrating available patient data. CleftGAN not only addressed the shortage of clinical cleft datasets but also opened new opportunities for developing high-quality data resources for research and treatment.

### Speech-language therapy

Children with CL/P often present with a speech disorder known as hypernasality, which results from velopharyngeal insufficiency (VPI) and adversely affects both speech intelligibility and voice quality. Whisper (OpenAI) applied large language models to develop an algorithm for detecting hypernasality from speech, achieving an accuracy of 97 %.<sup>33</sup> Beyond diagnosis, the Objective Hypernasality Measure model was trained on normal speech data to quantify the severity of hypernasality and demonstrated strong correlation with expert evaluations ( $r > 0.7$ ).<sup>18</sup> Saxon et al. applied ML using a Hidden Markov Model-Gaussian Mixture Model framework to extract acoustic features from speech.<sup>37</sup> Interestingly, although these features were initially derived from hypernasal speech in Parkinson's disease, the model was still able to identify hypernasality in CL/P children, despite the entirely different underlying mechanism of VPI.

From another perspective, Ha et al. developed a DL diagnostic system utilizing videofluoroscopy to detect VPI in CL/P patients. The results demonstrated high accuracy,

with ResNet and Xception identified as the most effective models for VPI diagnosis.<sup>35</sup> In addition to hypernasality, many children with CL/P also develop other speech disorders, such as pharyngeal fricatives—an atypical sound produced in the pharyngeal region to compensate for the lack of oral pressure. Using a Decision Tree algorithm, He et al. proposed an acoustic analysis method to automatically detect pharyngeal fricatives.<sup>20</sup> The system achieved effective discrimination with an accuracy of 88–89 % and an overall model performance of 93 %. Another study introduced the Objective Articulation Measure, a framework for evaluating speech production through consonant–vowel transition analysis.<sup>36</sup> This model performed well for children with CL/P and showed a high correlation with conventional perceptual assessments.

Another investigation examined the re-identification risk of pathological speech, including CL/P, using a DL-based automatic speaker verification system. Despite atypical acoustic features, the system was still able to achieve recognition accuracy comparable to normal speech under certain conditions, while in other settings the re-identification risk was even higher.<sup>38</sup> The authors concluded that voices of individuals with CL/P may serve as identifiable markers, thereby compromising speaker anonymity. To mitigate this risk, Tayebi Arasteh et al. employed DL-based anonymization using the McAdams Coefficient, which significantly reduced speaker identifiability (by up to 1933 %) while preserving data utility for clinical analysis.<sup>34</sup>

### Caregiver education

Caring for children with CL/P requires continuous education and support from both families and medical staff. Mahedia et al. suggested that ChatGPT could assist in postoperative counseling by providing responses that are not only consistent with clinical guidelines but also tailored to the patient's clinical status.<sup>58</sup> Similarly, Chaker et al. reported that ChatGPT reduced the time and effort needed to develop educational resources and was able to correctly respond to 13 commonly asked postoperative care questions with an accuracy of approximately 69 % compared with expert responses.<sup>59</sup>

In addition, assessing patient-reported outcomes is essential for optimizing care in children with CL/P. The CLEFT-Q is widely used to evaluate quality of life in the post-treatment phase; however, its length can make it burdensome for children. Computerized adaptive testing (CAT) has been shown to effectively shorten the questionnaire while maintaining accuracy. More recently, Harrison et al. applied a Decision Tree algorithm to integrate clinical variables for further optimization of this process.<sup>60</sup> While CAT remained superior, the study highlighted the potential of ML for future applications in polytomous data systems.

### Risk prediction

Several studies have shown that the etiology of CL/P arises from complex interactions between genetic and environmental factors. Accordingly, Shafi et al. developed a Multilayer Perceptron neural network model to predict the



prenatal risk of CL/P.<sup>57</sup> The model demonstrated promising performance, achieving an accuracy of up to 92.6 %, and identified several relevant risk factors, including family history of CL/P, pregnancy loss, and parental smoking habits. In the postnatal stage, another study applied logistic regression (LR) algorithms to construct a model predicting the risk of future orthognathic surgery in children with CL/P.<sup>56</sup> Significant prognostic factors included the number of clefts, male sex, and the palatal closure technique. This model achieved high predictive performance, with an AUC of 0.9.

## Genetic and molecular approaches

Currently, non-invasive tests such as maternal serum analysis have emerged as promising methods to support the early diagnosis of CL/P. Jia et al. combined lipidomics with ML to screen potential lipid biomarkers for CLP.<sup>14</sup> In this study, feature-selection methods combined with the robust rank aggregation approach were applied to identify dysregulated lipids from untargeted lipidomics. Seven classification models were then evaluated, with Naive Bayes achieving the highest diagnostic performance and yielding a panel of 35 candidate lipid biomarkers. These candidates were subsequently validated through targeted lipidomics and multivariate analyses, resulting in a three-lipid panel: arachidonic acid (20:4), lysophosphatidylcholine (LPC, 18:0), and phosphatidylcholine (PC, 16:0e/22:0), which demonstrated excellent diagnostic accuracy (AUC = 0.97, sensitivity = 80 %, and specificity = 84 %). Importantly, arachidonic acid (20:4) and LPC (18:0) were also significantly downregulated in early maternal serum samples from the CL/P group in the additional validation cohort, further supporting their potential involvement in the etiopathogenesis of CL/P. PC plays a crucial role in lipid emulsification and metabolism and also serves as a source of lipid messengers.<sup>66</sup> The observed reduction in PC (16:0e/22:0) suggests diminished anti-inflammatory capacity during craniofacial development, potentially contributing to CL/P. LPC regulates cell function and exerts immunoregulatory effects by suppressing proinflammatory cytokines and enhancing anti-inflammatory mediators.<sup>67</sup> Reduced LPC (18:0) may impair these protective effects, creating a proinflammatory environment detrimental to lip and palate formation. Moreover, free fatty acids, particularly arachidonic acid (20:4), serve as important regulators of antioxidant signaling, inflammation, and neurodevelopment.<sup>68</sup> Imbalances in polyunsaturated fatty acids have been associated with adverse neurocognitive and craniofacial outcomes.<sup>69</sup>

Meanwhile, ML has also proven effective in assessing CLP risk based on genetic variants, particularly single nucleotide polymorphisms (SNPs). Zhang et al. validated 43 GWAS-derived SNPs and constructed predictive models using multiple ML algorithms and traditional risk scoring methods.<sup>43</sup> Notably, this study demonstrated that four SNPs located in *MTHFR* and *RBP4* genes involved in folic acid and vitamin A metabolism collectively contributed about 76.1 % to the predictive ability for CL/P risk (AUC = 0.761). Zhang's findings support that genetic diagnosis of *MTHFR* and *RBP4* variants using an ML approach may guide

nutritional intervention strategies to lower the risk of CL/P, consistent with evidence that adequate folic acid and vitamin A supplementation during conception reduces the likelihood of CL/P in offspring.<sup>70</sup> In the same domain, Kang et al. evaluated the predictive performance of a Genetic Algorithm-optimized Neural Network Ensemble (GANNE) against eight traditional risk classification methods. Results indicated that GANNE could automatically select the most relevant SNP groups, achieving an AUC of 88.2 % with a panel of 10 SNPs.<sup>40</sup> In addition, the functional annotation and protein–protein interaction (PPI) analyses showed that *IRF6*, the gene most often selected by GANNE, acted as a major hub gene, align with its key role in craniofacial development. Other genes, including *RUNX2*, *MTHFR*, *PVRL1*, *TGFB3*, and *TBX22*, were also involved in tissue growth and tooth formation, suggesting that the selected SNP panel has real biological meaning for predicting CL/P risk. In addition, González et al. developed TAGOOS, a supervised learning method that uses regulatory annotations to prioritize non-coding SNPs. Applied to cleft lip loci, TAGOOS confirmed known associations and also detected new regulatory regions enriched in transcription factors related to craniofacial development, thus providing biological insights and publicly available genome-wide scores for further research.<sup>42</sup> Xiao et al. applied gapped k-mer ML to integrate GWAS data with epigenomic profiles from oral epithelial cells, enabling the discovery of functional non-coding variants missed by traditional analyses.<sup>45</sup> Using this model, they prioritized sub-threshold GWAS SNPs that overlapped active enhancers and promoters, then combined 3D chromatin interaction data to link these variants to target genes involved in palatal development. Functional validation showed that several risk SNPs disrupted key transcription factor motifs, such as *SOX2*, revealing a regulatory mechanism that contributes to cleft pathogenesis.

ML has also been applied to explore gene–gene interactions in CLP development. Liu et al. used LR to identify significant interactions between *ACTN1* and *CTNBN1* in the cell adhesion pathway.<sup>41</sup> This antagonistic interaction indicates that the joint regulation of these genes in the adherens junction network could affect epithelial adhesion and palatal shelf fusion, contributing to CLP pathogenesis. Similarly, Li et al. applied ML and regression-based methods to uncover the role of the *WNT* gene family in defect formation.<sup>44</sup> They identified strong gene–gene interactions, including *WNT5B-MAFB* and *WNT5A-IRF6-C1orf107*. These findings underscore the biological significance of *WNT5B* as a signaling ligand involved in tissue development and longitudinal bone growth regulation, reinforcing its potential contribution to craniofacial morphogenesis. Dai et al. analyzed epigenetic data using a CNN algorithm and demonstrated that CLP-related SNPs exhibited high biological activity and dynamic changes across developmental stages.<sup>39</sup> The model quantified skull-related SNP activity and identified six high-risk variants with a clear linear relationship to craniofacial developmental progression, suggesting that these SNPs could play a temporal regulatory role. Furthermore, trophoblast cells were pinpointed by cell-type specificity analysis as having the highest enrichment of orofacial cleft-related risk signals.

## Discussion

This review highlights the rapid expansion of artificial intelligence applications in CL/P management. The analysis revealed that imaging diagnosis accounted for the largest number of studies, followed by speech-language therapy and genetic or molecular approaches, while risk prediction and caregiver education were relatively underrepresented. This distribution reflects both the availability of data sources and the immediate clinical needs in CL/P care. Imaging data such as ultrasound, panoramic radiographs, and CBCT are abundant and routinely collected in clinical practice, which facilitates AI model development. In contrast, studies on caregiver education or risk prediction require longitudinal data and patient-reported outcomes, which are more difficult to obtain, explaining their limited presence in literature. In addition, several review articles provided comprehensive perspectives, further supporting the potential of AI integration across multiple aspects of CL/P care.

The clinical implications of these findings are considerable. AI-assisted imaging diagnosis has demonstrated high sensitivity and specificity, sometimes outperforming expert clinicians, and could shorten examination times and reduce inter-operator variability. Similarly, AI applications in speech-language therapy provide objective tools for detecting hypernasality, articulation errors, and velopharyngeal insufficiency, offering support to speech pathologists and enabling more standardized assessments. In surgical intervention, deep learning models are beginning to support both planning and evaluation, with generative approaches such as CleftGAN showing promise for addressing the shortage of clinical datasets. These advances collectively indicate that AI can reduce the workload of clinicians, improve diagnostic accuracy, and enhance patient outcomes. AI-assisted intraoral scanning and 3D model reconstruction also demonstrated promising accuracy and cost-effectiveness, particularly for designing preoperative orthopedic plates in low-resource settings.

At the same time, several challenges remain. First, most AI models in CL/P are trained and validated on relatively small, single-center datasets, which limit their generalizability across diverse populations and healthcare systems. Second, although imaging and speech data are relatively well represented, integration with genetic, molecular, and environmental factors is still in its infancy, despite the potential of such multimodal approaches to improve risk prediction and personalized care. Third, ethical concerns, especially those related to data privacy and potential patient re-identification, are critical issues that must be addressed before AI can be safely implemented in routine clinical practice.

Future directions should focus on large-scale, multi-center collaborations to build diverse and high-quality datasets that enable robust model validation. Efforts should also be made to develop multimodal models that combine imaging, genetic, molecular, and clinical data for comprehensive patient assessment. Furthermore, clear ethical and regulatory frameworks must be established to ensure patient privacy, data security, and the safe deployment of AI tools in clinical practice. To achieve these

goals, multi-center data sharing frameworks are a practical next step. Such frameworks allow different research centers to collaborate while safeguarding patient privacy and data integrity. Two major strategies have emerged in this context: centralized and federated approaches. A centralized approach, in which data are pooled into a single repository for model training and validation, can create large, harmonized datasets that improve generalizability. However, it requires robust governance and secure infrastructure to minimize risks related to data transfer and potential breaches. By contrast, federated learning offers a decentralized solution where models are trained locally on-site, and only model parameters, not raw patient data, are shared with a central server for aggregation. This approach preserves patient privacy, mitigates regulatory barriers, and can be particularly effective in contexts where cross-border data sharing is challenging. Together, these strategies could help overcome current barriers to data scarcity and reproducibility, ultimately paving the way for practical implementation in the near future.

In summary, AI is gradually reshaping how clinicians approach the diagnosis, treatment, and care of individuals with CLP. AI-facilitated tools not only enhance clinical efficiency but also help reduce time, effort, and costs for patients. However, as a relatively new technology, many AI models have not yet been fully validated, particularly in developing countries where resources and data remain limited. The lack of high-quality training datasets further reduces the generalizability of these models. Ethical issues also require careful attention, as sensitive patient data may inadvertently compromise personal identity. Despite these challenges, AI demonstrates strong potential due to its ability to learn autonomously and address a wide range of complex problems, offering an innovative strategy for CLP management. Future research should focus on well-designed studies to clarify the long-term benefits and limitations before AI can be widely implemented in clinical practice.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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