Emerging Digital and Regenerative Approaches in Cleft Lip and Palate Management

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Abstract
Care for Cleft lip and palate is still a challenging and lengthy procedure that requires constant communication among patients, caregivers, and interdisciplinary teams. Treatment planning, monitoring, and outcome assessment in cleft care have been significantly enhanced over the past few decades, owing to the developments in diagnostic tools. Presurgical orthopedic procedures have been completely transformed by the incorporation of digital technologies, which have improved clinical precision and simplified appliance fabrication. Similarly to this, the introduction of clear aligner therapy has widened the number of orthodontic treatment choices available to patients with clefts by providing aesthetically appealing and minimally invasive alternatives for conventional techniques. Stem cell based therapy is a promising regenerative method for restoration of oral and maxillofacial structures. Together, these developments mark an important milestone in cleft care that is more tailored, effective, and biologically driven.

Keywords: Cleft lip, Printing, Three-Dimensional, Cleft palate, Artificial Intelligence, Tissue engineering, Nasoalveolar Molding

Introduction

The most common type of congenital craniofacial anomaly is orofacial clefting[1,3]. It is characterized by one or more clefts or discontinuities within the structures of the oral cavity, face, or cranial base present at birth [1,3]. Normal feeding, speech, facial growth, and facial esthetics can be achieved by early reconstruction [3]. Beginning at birth and continuing into adulthood, cleft patients often require extensive orthodontic and surgical management [1].

Timely orthodontic interventions should be planned, and each intervention must have organized treatment goals [2]. In cleft patients, the goal is to enhance treatment outcomes with minimal intervention for complete recovery [2]. To improve patient care and management among individuals with orofacial clefting, an interdisciplinary team is considered to be an essential tool [3]. Increasing use of novel tools like Artificial intelligence, 3D printing, Clear aligners, and stem cells have established higher standards of personalized and minimally invasive treatment. This review sheds light on the recent technologies in cleft lip and palate therapy.

Historical Progression Of Diagnostics In Cleft Management

Management of orofacial clefting is a tedious procedure for both the patient and the orthodontist, involving regular follow-up, clear communication, and progress monitoring [4].The introduction of diagnostic aids like CBCT (Cone-Beam Computed Tomography) has allowed precise estimation of alveolar cleft volume, which in turn helps gauge the graft material requirements [5,6].

Newer innovations, including sophisticated 3D modeling techniques, have made it possible to perform detailed segmentation of both hard and soft tissues using CBCT and conventional CT scans [7] . Conventional impressions with alginate are associated with the possibility of retention of impression material and fragment aspiration, leading to inflammation in newborns and infants. Hence, intraoral scanning is now the preferred method [8] .

Accurate 3D models can be created using 3D printing, which has hopes to become a patient education tool and treatment planning [4].

Improvements In Cleft Treatment Techniques And Approaches

Distraction osteogenesis became an important part of cleft management as patients who underwent nasolabial surgery previously reported with speech and facial deformities. It is used to treat cleft and syndromic patients. Osteotomy is done to create bone segments which is separated and later stimulated to form new bones which lengthen it [4]. To ensure selective movement of specific tooth without repercussions on the neighbouring teeth, temporary anchorage devices or mini screws were developed [9].

Integration of Artificial Intelligence in Cleft and Craniofacial Care [3]

Progress of AI in Healthcare and Cleft Management

Artificial intelligence (AI) is reshaping modern healthcare by employing the potential of large datasets, machine learning, and predictive algorithms to enhance diagnostic accuracy, personalize treatment strategies, and optimize patient outcomes [10]. AI integration presents innovative opportunities to improve orthodontic management, surgical planning, early diagnosis, and overall patient care in the field of cleft and craniofacial anomalies (CFAs). This amalgamation creates the opportunity to improve the quality of life for affected individuals while mitigating the psychosocial burden borne by their families [10].

AI in Early Diagnosis and Risk Prediction of Cleft Anomalies

In present times , Artificial intelligence (AI) is being used in the detection of cleft lip and palate. Based on the existence of clefts, artificial intelligence (AI) has been used to categorize foetal ultrasound images and differentiate between pathologic and normal cases. AI models that combine convolutional neural networks (CNN) and support vector machines (SVM) have successfully detected clefts in infants, even distinguishing between unilateral and bilateral clefts by utilizing frontal digital photos. Neural networks have also been used to estimate cleft volumes preoperatively by reconstructing defects from imaging data to help with surgical planning [11].

AI applications have expanded beyond image analysis to include genetic risk prediction. The possibility of cleft palate and lip can be predicted with the help of AI by using genetic and environmental data. The use of AI to assess the risk of developing CLP may improve treatment strategies, early detection, and preventative measures. In addition to extrinsic risk factors such as maternal smoking and folic acid deficiency, CLP is associated with mutations in genes such as IRF6, MSX1, TBX22, and locations on chromosomes 1, 2, 8, and 17. These advanced AI algorithms can combine genetic information with environmental and demographic data to create accurate risk forecasting models [10].

AI in Orthodontic Decision-Making for Cleft Patients

AI-based decision support systems have demonstrated remarkable promise in augmenting orthodontic planning. Orthodontic intervention is critical to the comprehensive management of CLP, particularly following secondary alveolar bone grafting. Traditionally, clinical expertise has played a major role in treatment planning [10].

Early models by Takada and Yagi achieved 86–90% concordance with expert clinical judgments using standardized diagnostic data. Subsequent advancements, such as the artificial neural network (ANN) model by Xie et al., achieved 80% accuracy in distinguishing extraction from non-extraction cases. Jung and Kim's development of an extraction prediction model using R programming demonstrated 93% accuracy in identifying extraction cases and 84% accuracy in overall treatment planning. More recently, Li et al. reported a 94% accuracy rate for extraction need prediction, with key determinants including the curve of Spee, ANB angle, and maxillary arch crowding [10].

These findings underscore the potential of AI to serve as a reliable adjunct in orthodontic treatment planning for CLP patients, offering enhanced precision and consistency.

AI-Assisted Surgical Planning and Preoperative Assessments

AI-driven imaging analysis has further revolutionized surgical planning for cleft repair. Neural network models have been employed to reconstruct three-dimensional cleft defects from imaging data, facilitating accurate preoperative volume estimations. These predictive reconstructions assist surgeons in strategizing optimal grafting and closure techniques, potentially enhancing surgical precision and reducing postoperative complications.

The use of AI in surgical planning has produced encouraging outcomes. Choi et al. developed a deep learning-based model that stratified surgical versus non-surgical cases with an overall diagnostic accuracy of 96% [11].

The model achieved perfect accuracy in identifying surgical needs in Class II and III malocclusions. Nevertheless, this prototype's performance was heavily influenced by heterogeneity of the training dataset, highlighting a need for broader validation [12].

Similarly, Shin et al. utilized deep learning algorithms to diagnose skeletal malocclusions by analyzing transverse and longitudinal cephalograms, achieving a diagnostic accuracy of 95.4%, with a sensitivity of 84.4% and specificity of 99.3%. In spite of these positive results, Shin's model is likewise limited by its exclusive focus on a specific ethnic cohort, necessitating further research across diverse populations [13].

Although these studies emphasize the influence of AI in enhancing decision-making for the orthodontic and surgical treatment of patients with orofacial clefts [3], several challenges remain to be addressed. In particular, there is still work to be done in using AI to guide growth modification treatments and ensure that models perform well across different ethnic and demographic groups. Future research should concentrate on developing and validating AI models with diverse, multiethnic datasets to improve AI's application in cleft care [10].

Table 1: Types of Intervention

TYPE OF INTERVENTION	TRADITIONAL APPROACH	DIGITAL APPROACH	MAIN DISTICTION
Cephalometric analysis	Manual landmark identification and measurement	AI assisted landmark detection and analysis	Rapid analysis and potential for improved accuracy

Diagnosis and treatment prediction	Clinical examination and experience based prediction	AI/ML assisted diagnosus and outcome prediction	Enhanced precision in diagnosis ,improved treatment planning

3D Printing and Digital Workflows in Cleft Care

The introduction of 3D technologies has led to significant improvements in NAM therapy. Stereophotogrammetry, a form of 3D photography, has been employed to quantitatively assess the gradual morphological changes that take place during treatment [14]. The incorporation of computer-aided design and computer-aided manufacturing (CAD/CAM) in the creation of NAM appliances has created a production process that is cost-effective, efficient, and more user-friendly compared to traditional methods [14,15].

Numerous studies have highlighted the effective use of rapid prototyping and CAD/CAM additive manufacturing in the production of adaptable and structurally robust NAM appliances [14]. Recent findings suggest that 3D-printed NAM appliances can help shorten appointment times, enhance accuracy, and lower costs associated with various 3D fabrication techniques [14]. Multiple intraoral molding plates can be created from a single impression by combining a graphical user interface and CAD -CAM technology. For instance, in 2017, Bauer et al. introduced the RapidNAM system, which uses a "growth prediction factor" to foresee cleft growth in patients and produce a series of molding plates accordingly [14,16]. Furthermore, a 2018 study by Grill et al. utilized RapidNAM to facilitate the transfer of nasal stents among different intraoral molding plates [17]. Zheng et al. innovated a split-type 3D-PNAM device, which divides the nasal and alveolar segments to minimize negative mechanical interactions. This design led to enhancements in arch form, a reduction in cleft width, and better nasal morphology, resulting in fewer required clinical interventions [18].

Employing principles of clear aligners, Bous et al. explored the use of digital technologies in presurgical orthopedics [18]. They implemented a fully digital workflow that allowed for the sequential repositioning of alveolar segments using customized thin aligner plates. Despite a few minor variations in segment placement, the general benefits of utilizing technology have been significant [18].

3D technologies enhance procedural efficiency and have contributed to important patient-centered improvements. Previously common complications, like mucosal irritation, have been significantly reduced by digital workflows. It also reduces the burden on the caregivers, thus making the treatment a better experience. However, muscosal ulceration still occurs, but these can be managed better due to the precision of 3D printed devices [14].

Figure 1: Projected Movements Demonstrated By Successive Maxillary Casts And Nams [14]

Clear Aligners in cleft patients

Clear aligners were introduced by Align technology in 1997, which had revolutionized orthodontics. It is equivalent to previously used braces to move teeth and alveolar segments laterally [3].

Clear aligner therapy provided a patient-friendly and comfortable option in presurgical infant orthopedics. It offers the advantage of fewer visits as the molding process is more simplified and does not require the lab procedures used in the Grayson technique. It is also not accompanied by risks associated with acrylic plate including ulcers and lacerations, thus, it provides a convenient option for patient and caregiver [19] .

Clear aligner therapy is a valid treatment for expansion and dental alignment. Although it may not be appropriate in patients with multiple missing short and/or mobile teeth, multiple steel crowns, severe ectopic eruption, or in with poor compliance, it still has many advantages [20]. They offer less noticeability, improved oral hygiene, shorter appointments, and fewer emergencies [20].

The digital workflow allows for more precise arch coordination and tooth movement. Premaxillary intrusion and postsurgical retention can also be achieved with the help of clear aligners [1].

Role of Regenerative medicine in Cleft Care

"Stem cells" are pluripotent cells that can differentiate into specialized cells with specialized effector functions. Possible applications include the rehabilitation and reconstruction of tissues and organs [21,22].

Successful regeneration of oromaxillofacial structures has been achieved by stem cell therapy. Intense research on mesenchymal stem cells in the past decade. Osteoblastic, adipogenic, and chondrogenic cell lines can be created from bone marrow, dental pulp, umbilical cord blood, and adipose tissue [22].

Previously used graft therapies may be substituted in the future by bone regeneration using stem cells [23].

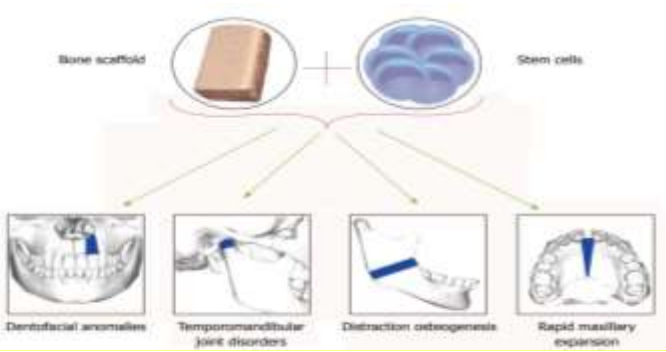
Mesenchymal stem cells (MSCs) is an emerging field of research currently in the limelight. Various approaches include direct implantation at the defect site or by providing scaffolds as a support. The osteoconductive scaffold and osteoinductive growth factors promote the differentiation of MSCs into osteogenic cells [24].

With success rates as high as 88%, autogenous cancellous bone grafting—especially from the anterior iliac crest—remains the gold standard for reconstructing alveolar cleft [3,22,24].

Regarding the extent of regeneration, Behnia et al. demonstrated 50% filling of the bone defect within three months of the procedure [25]. Regeneration up to 79.1% was reported in a study by Hibi et al [22,26].

Compared to autogenous bone grafting, the use of stem cells can alleviate defect size through the formation of bone, have less postoperative morbidity, and enable the teeth in the affected area to erupt in correct location. It is also associated with reduced inflammation and scars [22,24,27].

Figure 2: Stem Cells In Orthodontics [24]



Current Limitations and Future Perspectives

Significant progress has been made in the use of Artificial intelligence, stem cell therapy, clear aligners, and 3D printing. Standardised protocols are yet to be established, which leads to varying treatment approaches and effectiveness. Economic feasibility is yet to be proven due to a lack of cost-effective analysis. Due to the lack of data, new research on long-term treatment outcomes and patient-centered care is of paramount importance. To improve the quality of life in those with cleft anomalies, more studies on the safety and effectiveness of these methods must be done.

Conclusion

An interdisciplainary team of surgeons, orthodontists, speech therapists, and psychologists is required for holistic management of cleft lip and palate. To predict outcomes and personalize orthodontic care, integrating artificial intelligence offers new possibilities. Regenerative medicine and stem cell therapy are promising novel techniques to enhance tissue healing and bone regeneration. Digital technologies, such as 3D printing and clear aligner therapy, are reshaping treatment protocols, reducing patient burden, and improving efficiency. Future progress relies on translating scientific discoveries into clinical practice, incorporating new technologies, and maintaining a strong focus on comprehensive patient-centered care.

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