UNIVERSIDADE DE SÃO PAULO
HOSPITAL DE REABILITAÇÃO DE ANOMALIAS CRANIOFACIAIS

ISABELLA SIMÕES HOLZ

Permanent Canine Eruption Into The Grafted Alveolar Cleft Region: Are There Predictor Factors For Impaction?

Comportamento do canino permanente na área da fissura alveolar após enxerto com proteína morfogenética óssea (rh-BMP2)

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Dissertação apresentada ao Hospital de Reabilitação de Anomalias Craniofaciais, Universidade de São Paulo, para obtenção do Título de Mestre em Ciências da Reabilitação.

Área de concentração: Fissuras Orofaciais e Anomalias Relacionadas

Orientadora: Prof. Dra. Daniela G. Garib
Co-Orientadora: Dra. Roberta Martinelli Carvalho

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Holz, Isabella Simões
H748 Permanent Canine Eruption Into The Grafted Alveolar Cleft Region: Are There Predictor Factors For Impaction?/ Isabella Simões Holz. Bauru, 2017.
55p.; il.; 30cm.

Dissertação (Mestrado– Área de Concentração Fissuras Orofaciais e Anomalias Relacionadas) – Hospital de Reabilitação de Anomalias Craniofaciais, Universidade de São Paulo.

Orientador: Daniela Gamba Garib Carreira
Descritores: 1. Alveolar bone grafting 2. Tooth eruption 3. Canine impaction

FOLHA DE APROVAÇÃO

Dissertação apresentada e defendida por Isabella Simões Holz e aprovada pela comissão julgadora em ____/____/____.

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Data de depósito da dissertação junto à SPG ___/___/___

DEDICATÓRIA

Dedico este trabalho aos pacientes do Centrinho-USP, beneficiados pelas brilhantes pesquisas realizadas no Hospital.

AGRADECIMENTO ESPECIAL

À Profa. Dra. Daniela Garib, por esse lindo projeto. Sinto-me privilegiada em concluir um mestrado sob sua orientação.

Agradeço por me apresentar esse lindo universo da pesquisa.

Obrigada pelos ensinamentos, pela paciência, convivência, acolhimento e por todo seu empenho para realização deste trabalho. Estendo o agradecimento ao Alemão e as lindas Helena e Laura.

AGRADECIMENTO ESPECIAL

Ao meu mestre, Dino Capelozza, que me apresentou a Ortodontia e me despertou esse carinho e paixão pelo Centrinho.

Sem o senhor, nada disso seria possível.

Obrigada pelos ensinamentos, pela convivencia, pelo apoio e por fazer da Ortodontia essa especialidade tão inspiradora.

AGRADECIMENTO ESPECIAL

À minha mãe, eterna incentivadora.
Obrigada por fazer qualquer sonho possível.
Obrigada pelos ensinamentos, pela convivência e por todos os esforços para que eu tivesse a melhor educação possível.
Obrigada por ser esse exemplo de força e determinação.
Obrigada por ser a minha mãe.

AGRADECIMENTO ESPECIAL

Ao meu pai, meu eterno amor. Obrigada pelos ensinamentos e ser um exemplo de dignidade, ética e caráter. Obrigada por na sua presente ausência, incentivar na minha formação.

AGRADECIMENTOS

A Deus por todas as bençãos concedidas. Obrigada por me possiblitar a realização de mais um sonho. Que eu possa ser merecedora de todas as coisas boas que me acontecem!

Ao meu irmão Gustavo, por ser o melhor irmão do mundo. Obrigada pelo apoio, incentivo e por me fazer ser uma pessoa melhor. Obrigada pela convivencia e por também tornar esse sonho possivel.

Ao meu amigo e companheiro Fabio, por todo apoio. Obrigada pelo incentivo, pela convivencia e por fazer a minha vida mais feliz. Você é o motivo da minha inspiração.

A minha familia, tios, primos, por sempre me apoiarem em tudo e entenderem a minha ausencia nesse periodo.

Ao professor Steven Lindauer, pelo receptividade e acolhimento. Obrigada pelos ensinamentos e pela brilhante participação neste estudo. A sua contribuição foi extremamente enriquecedora.

À Fatima Capelozza, obrigada pela convivencia e por sempre me acolher e receber tão bem quando em Bauru. A senhora estará guardada sempre em meu coração. Estendo o meu agradecimento a sua linda familia.

A querida amiga Aura, por tornar os momentos em Bauru, muito mais leves e divertidos. Obrigada pela amizade, convivencia e toda ajuda durante essa jornada.

A minha sócia e amiga Letícia Aguiar, por tornar esse posível. Obrigada pelo apoio, pela amizade e pela convivência. Você é muito especial.

Aos amigos José, Cláudia e Luiza Capellozza, pela convivencia. Obrigada por toda ajuda, apoio, acolhimento. Obrigada por fazer os momentos em Bauru tornarem-se mais leves. Vocês são pessoas muito especiais que estarão sempre em meu coração.

A amiga Claudia Leal, obrigada por todo apoio, e por aceitar fazer parte dessa pesquisa. Você foi fundamental para a realização deste trabalho.

Ao amigo Zezinho, pela amizade. Obrigada pelo apoio, convivencia e atenção. Obrigada por estar sempre presente e pronto para ajudar.

Ao amigo Guilherme Capelozza, por tudo. Obrigada pelos momentos divertidos, pela amizade, acolhimento e por tornar os momentos em Bauru muito mais alegres.

Ao amigo Alexandre Magno, pela doce amizade. Obrigada por fazer parte da minha vida e me incluir em tantos projetos bacanas. Obrigada pela convivencia.

A amiga Érika pelo acolhimento e amizade. Obrigada pelo apoio e por toda ajuda durante o mestrado.

Aos amigos Fernando e Isabela, pela amizade e convivencia.

Aos amigos Oscar e Martha, pela amizade e convivência. Conhecer vocês foi um presente!

Aos amigos Arthur e Olga, pela amizade. Obrigada por se mostrarem sempre prestativos e pela doce convivencia.

Aos amigos Alexandre Ribeiro e Bruno Dias, pela convivencia nessa jornada. Obrigada pelo apoio e ajuda durante o mestrado.

Ao Prof. Dr. José Roberto Pereira Lauris, por toda ajuda. Obrigada pela paciência em realizar a estatística deste trabalho.

A Prof. Dra. Rita Lauris pelos ensinamentos e convivência. Você é a pessoa mais doce que conheço.

A Roberta Martinelli, pela orientação. Obrigada por toda ajuda durante este trabalho.

Ao Dr. Reinaldo Mazottini, pelo prazer da convivencia. Obrigada pelos ensinamentos e pela paixão pelo HRAC.

Aos amigos e colegas da Pós Graduação, pela convivencia. Obrigada por dividir conhecimentos e tornar os momentos mais divertidos.

Aos amigos que a Odontologia me deu, Ana Cláudia e Paulo Conti, David e Thiene Normando. Obrigada pela convivencia e por todos os momentos de aprendizado e divertimento.

Ao Fabricio Rodrigues, por toda ajuda e por tornar sempre nossas apresentações mais atraentes.

Ao Rinaldo, por todo empenho e paciencia. Obrigada por toda ajuda e por ajudar a levantar grande parte da minha amostra. Você foi fundamental para a realização desse projeto.

Aos professores do setor de Ortodontia do HRAC, Araci, Aiello, Silvia, Terumi, Renata, Adriano, Tiago, Gleisieli e Rogério pelo acolhimento e todo conhecimento compartilhado.

Aos professsores da Pós Graduação do HRAC, por todos os ensinamentos. Vocês foram fundamentais para a minha formação.

As funcionárias da Pós Graduação, Zezé, Tati e Lucy e Aninha, por toda ajuda, paciencia, atenção e carinho.

Aos residentes de Ortodontia do HRAC-USP, pelo acolhimento e convivencia.

Às auxiliares Denise, Soninha, Rosangela, Suzana, Solange, Leila, Sabrina e Celina pelo acolhimento e convivencia.

Às meninas da APG, pela determinação e convivencia. Obrigada por ajudar a fazer do Centrinho, um lugar ainda melhor.

A todos os funcionários do HRAC-USP, por fazerem desse hospital um lugar tão lindo e acolhedor. Vocês foram fundamentais para que a minha paixão pelo centrinho aumentasse ainda mais.

Aos pacientes do HRAC-USP por fazerem meus dias melhores e por me despertar o sentimento de ser uma pessoa melhor.

À Capes, pela bolsa de estudos.

A todos que colaboraram indiretamente para a conclusão desse trabalho, muito obrigada.

ABSTRACT

Background: Predictor factors for early diagnosis of maxillary canine impaction (Mx.CI) in unilateral complete cleft lip and palate (UCLP) have not yet been clearly described in the literature. **Objectives:** The aim of this study was to investigate the eruption pattern of maxillary permanent canines in the alveolar cleft area before and after the secondary alveolar bone grafting (SABG) and to assess the risk indicators for canine impaction and its association with other dental anomalies. **Methods:** The sample consisted of 75 patients with UCLP who underwent SABG with rhBMP-2 with a mean age of 9.8 years of age at a single center. The study design was a split mouth with the non-cleft hemi-arch comprising the control group. Panoramic radiographs taken before (T1), immediately after (T2) and one year after SABG (T3) were used to assess the following parameters in both cleft (CS) and non-cleft (NCS) sides: canine mesiodistal angulation, canine height relative to the occlusal plane and canine mesial displacement and superimposition with the neighboring maxillary incisors. The frequency of associated dental anomalies including agenesis, transposition and distoangulation was compared between patients with and without canine impaction at the CS. The measures were carried out with Dolphin Imaging software, version 10.5 (Dolphing Imaging, Charsworth, CA, USA). Comparisons of canine positional parameters between all three time points was performed using ANOVA. Comparisons of canine positional parameters between CS and NCS and between impaction and non-impaction cases were performed respectively using paired and independent t-tests. Comparisons for the frequency of associated dental anomalies between impaction and non-impaction cases as well as the association between canine mesial displacement and impaction at the CS were assessed using Fisher test. The significance level regarded was 5%. **Results:** The prevalence of canine impaction at the CS was 24%**.** Canine positional parameters were statistically different between CS and NCS. Canines at the CS were usually more mesially angulated and more distant from the occlusal plane when compared to NCS. At the CS, canines that became impacted showed an increased angulation and height from the occlusal plane compared to canines with spontaneous eruption at all time points (T1, T2 and T3). An increased prevalence of lateral incisor agenesis at CS (72.2%) was observed in the

subgroup with canine impaction compared to cases with canine spontaneous eruption (33.3%). No association between CS canine impaction and mesial displacement (zones) was found at any time point. **Conclusions:** Impacted canines at the CS in UCLP show an increased mesial angulation and an increased distance from the occlusal plane since the pre bone graft phase. The mesial displacement and superimposition with neighboring incisors should not be used as predictor factors for canine impaction in UCLP.

Key-words: alveolar bone grafting; Cleft Lip; Cleft palate; Tooth eruption; Impacted tooth

RESUMO

Introdução: Referenciais para um diagnóstico e intervenção precoce ainda não foram descritos em pacientes com fissuras labiopalatinas (FLP). **Objetivos:** O presente trabalho tem como objetivo investigar o padrão de irrupção do canino superior permanente na área da fissura antes e após o procedimento de enxerto alveolar com proteína óssea morfogenética (rhBMP-2) e avaliar os indicadores preditivos da impacção do canino permanente. **Materiais e métodos:** A amostra foi constituída de 75 pacientes com fissura labiopalatina completa e unilateral (FLPU) que foram submetidos ao enxerto ósseo secundário com rhBMP-2, em um único centro de reabilitação. Radiografias panorâmicas pré (T1), imediatamente após (T2) e um ano pós enxerto ósseo alveolar (T3) foram utilizadas para avaliar os seguintes parâmetros no lado com (LF) e sem fissura (LSF): angulação do canino, altura da coroa e deslocamento mesial do germe, presença de outras anomalias dentárias incluindo agenesias, distoangulação e transposição. As medidas foram realizadas com o programa Dolphin Imaging software, versão 10.5 (Dolphing Imaging, Charsworth, CA, USA). A comparação entre os três tempos foi realizada pelo teste ANOVA. A comparação dos parâmetros posicionais do germe dos caninos entre o lado com e sem fissura, bem como entre os casos em que os caninos irromperam espontaneamente e os que ficaram impactados, foi realizada por meio do teste t pareado e t independente, respectivamente. A comparação da prevalência de anomalias dentárias em pacientes com e sem caninos impactados foi realizada pelo teste de Fisher. O nível de significância adotado foi de 5%. **Resultados:** A prevalência de impacção de caninos no LF foi de 24%. Os parâmetros posicionais apresentaram diferenças estaticamente significativas entre os LF e LSF. Caninos do LF apresentaram-se mais angulados e mais distantes do plano oclusal em comparação ao LSF. Os caninos impactados do LF apresentaram maior angulação e distancia em relação ao plano oclusal quando comparados aos que irromperam espontaneamente entre os três tempos (T1, T2 e T3). Foi observada uma prevalência aumentada de agenesia do incisivo lateral superior no LF (72.2%) no subgrupo com caninos impactados comparado aos caninos com irrupção espontânea (33.3%). Não houve associação entre o deslocamento mesial (zonas) e impacção de caninos nos três tempos. **Conclusão:** Caninos impactados no LF apresentam angulação

aumentada e maior distancia do plano oclusal prévio ao enxerto. O deslocamento mesial e sobreposição dos incisivos adjacentes não devem ser utilizados como fatores preditivos de impacção em pacientes com FLPU.

Palavras-chave: Canino permanente, fissura alveolar, proteína morfogenética óssea

LIST OF ILLUSTRATIONS

LIST OF TABLES

TABLE OF CONTENTS

1 INTRODUCTION

1 INTRODUCTION

Cleft lip and palate represent the most prevalent craniofacial anomaly in humans and occurs with an average prevalence of 1 individual per 1000 births (WHO, 2002). In Brazil, it is assumed that the prevalence of cleft lip and palate oscillates around 1:650 (TRINDADE, IEK; SILVA FILHO, OG, 2007)

Currently, cleft lip and palate rehabilitation protocol includes secondary alveolar bone graft performed in late mixed dentition prior to eruption of the permanent canine (ENEMARK, 1985). Alveolar bone graft can be performed with autogenous bone from the iliac crest, chin or skullcap. Additionally, recombinant human Bone Morphogenetic Protein (rhBMP-2) is an option for autogenous bone graft (CARVALHO, 2011). Bone Morphogenetic Proteins (BMPs) are a group of proteins belonging to the TGF-beta of growth factors superfamily and are involved in embryonic development and formation of the skeleton. The rhBMP-2 in resorbable collagen membrane is a treatment option in the repair of alveolar cleft which exclude the need of a donor area, reducing surgical morbidity and postoperative discomfort (DINCKINSON et al, 2008).

The anatomical and functional adaptation observed in the grafted area allows the spontaneous migration and eruption of the adjacent maxillary canine. A parameter to evaluate the success of alveolar graft is the eruption pattern of the permanent canine (OBEROI et al., 2010). The maxillary canines usually develop above the other permanent teeth in the alveolar process. Thus, describe a longer and lasting eruption path, which makes it more susceptible to ectopic eruption. During spontaneous eruption, the canine moves toward the occlusal plane and gradually uprights. The prevalence of ectopia and impaction of maxillary canines in non-cleft population is equivalent to an average of 1.7% (ERICSON and KUROL, 1986). Studies have reported that autogenous bone graft before the eruption of permanent canine allows spontaneous migration of the permanent canine through the grafted area in about 23% to 97% of cases (HOGAN et al, 2003, JESUINO et al, 2010; MATSUI et al, 2005; SILVA FILHO et al, 2000). However, there is a percentage of 12-35% of maxillary canines that remain retained in the grafted area (RUSSELL and McLEOD, 2008; OBEROI et

al, 2010). The surgical exposure followed by orthodontic traction of the retained canine is the preferred treatment in these cases (FLEMING et al, 2009).

In patients without oral clefts, impacted canines can be early diagnosed through clinical exams associated to panoramic radiographs. Clinical examination can be carried out at the stage of "Ugly Duckling". Digital palpation of the alveolar process can reveal a buccal bulging of the permanent canine. If the canine cannot be palpated, a radiographic examination is necessary to complement the diagnosis. The panoramic radiograph reveals the position of the permanent canine in mesiodistal and vertical directions, long axis angulation, the degree of root development and its relationship with neighboring teeth (ERICSON and KUROL, 1986). The most widely used and reliable method for predicting canine impaction in patients without cleft was described by Lindauer and colleagues in 1992. The authors evaluated the relation between the canine cusp tip and the root of the permanent lateral incisor. The results showed that the greatest the proximity the cusp tip of the canine to the mesial region of the long axis of lateral incisor, the greater was the chance of canine impaction to occur. When the panoramic radiograph shows no overlap between the germ of the maxillary canines and the lateral incisor root, canine had a good prognosis to erupt spontaneously (LINDAUER et al, 1992). When diagnosed ectopic eruption of the maxillary canines in mixed dentition, some therapeutic approaches can be adopted to prevent impaction, such as extraction of the adjacent deciduous canine (ERICSON and KUROL, 1988), rapid maxillary expansion in order to generate transverse space for spontaneous eruption of the permanent canine (BACCETTI et al, 2009) and the use of appliances for distal movement of molars (head-gears) (ARMI et al, 2011).

Canine impaction in non-cleft patients is related to a genetic background (BECKER et al., 1981, 1999; ZILBERMAN et al., 1990; MOSSEY et al., 1994; BACCETTI, 1998; PECK et al., 1996) and is associated with other dental anomalies as tooth agenesis and small teeth (ANIC-MILOSEVIC, 2009; BECKER et al., 1981; PECK et al., 1996). However, factors that can contribute for a higher prevalence of impacted canines in unilateral cleft lip and palate (UCLP) are still unknown. Some authors associate impacted canines and the lack of bone in alveolar defect, which can reduce the available space in the jaw and result in canine displacement (TORTORA, 2008). Indeed, bone graft surgery to repair the cleft could interfere in permanent canine eruption (SEMB, 2012). Additionally, it has been suggested a positive relation between

tooth agenesis, clefting and genetic disturbances (LIDRAL, et al., 2008). Therefore, the means for diagnose maxillary canine impaction in patients without cleft are defined and well documented, which is evidenced by the abundance of studies in this area. However, in patients with cleft lip and palate - which have a prevalence of canine impaction 10 times higher, references for early diagnosis and intervention has not been yet described in literature. Consubstantiated by clinical relevance and the lack of studies relating the rhBMP-2 graft and canine impaction in patients with cleft lip and palate, this study analyzes the irruptive pattern of permanent maxillary canines in the grafted alveolar cleft as well as to evaluate the early radiographic indicators that could predict their impaction.

Canines that are impacted in patients with orofacial clefts already demonstrated bad tooth position prior to alveolar bone graft? What are the radiographic evidences to predict the retention of permanent canines in the cleft region? Canines would be impacted by the mechanical obstacle imposed by cleft and/or bone graft? Or retained canines represent a dental anomaly of genetic nature? All these questions are still with no evidence-based answers.

2 OBJECTIVES

2 OBJECTIVES

The aims of this study were:

1. To longitudinally assess permanent canine eruption path in the rh-BMP2 grafted alveolar cleft compared to antimere tooth at non-cleft side;

2. To evaluate early risk indicators of maxillary canine impaction at the cleft side;

3. To examine prevalence of dental anomalies associated with canine impaction in patients with UCLP.

3 ARTICLE

3 ARTICLE

Permanent canine eruption into the grafted alveolar cleft region: are there predictor factors for impaction?

Abstract

Background: Predictor factors for early diagnosis of maxillary canine impaction (Mx.CI) in unilateral complete cleft lip and palate (UCLP) have not yet been clearly described in the literature. **Objectives:** The aim of this study was to investigate the eruption pattern of maxillary permanent canines in the alveolar cleft area before and after the secondary alveolar bone grafting (SABG) and to assess the risk indicators for canine impaction and its association with other dental anomalies. **Methods:** The sample consisted of 75 patients with UCLP who underwent SABG with rhBMP-2 with a mean age of 9.8 years of age at a single center. The study design was a split mouth with the non-cleft hemi-arch comprising the control group. Panoramic radiographs taken before (T1), immediately after (T2) and one year after SABG (T3) were used to assess the following parameters in both cleft (CS) and non-cleft (NCS) sides: canine mesiodistal angulation, canine height relative to the occlusal plane and canine mesial displacement and superimposition with the neighboring maxillary incisors. The frequency of associated dental anomalies including agenesis, transposition and distoangulation was compared between patients with and without canine impaction at the CS. The measures were carried out with Dolphin Imaging software, version 10.5 (Dolphing Imaging, Charsworth, CA, USA). Comparisons of canine positional parameters between all three time points was performed using ANOVA. Comparisons of canine positional parameters between CS and NCS and between impaction and non-impaction cases were performed respectively using paired and independent t-tests. Comparisons for the frequency of associated dental anomalies between impaction and non-impaction cases as well as the association between canine mesial displacement and impaction at the CS were assessed using Fisher test. The significance level regarded was 5%. **Results:** The prevalence of canine impaction at the CS was 24%**.** Canine positional parameters were statistically different between CS

and NCS. Canines at the CS were usually more mesially angulated and more distant from the occlusal plane when compared to NCS. At the CS, canines that became impacted showed an increased angulation and height from the occlusal plane compared to canines with spontaneous eruption at all time points (T1, T2 and T3). An increased prevalence of lateral incisor agenesis at CS (72.2%) was observed in the subgroup with canine impaction compared to cases with canine spontaneous eruption (33.3%). No association between CS canine impaction and mesial displacement (zones) was found at any time point. **Conclusions:** Impacted canines at the CS in UCLP show an increased mesial angulation and an increased distance from the occlusal plane since the prebone graft phase. The mesial displacement and superimposition with neighboring incisors should not be used as predictor factors for canine impaction in UCLP.

Key-words: alveolar bone grafting; Cleft Lip; Cleft palate; Tooth eruption; Impacted tooth

Introduction

The prevalence of maxillary canine impaction in non-cleft population is equivalent to an average of 1.7%[1a, b]. In contrast, cleft lip and palate (CLP) patients present a percentage of 12-35% of maxillary canines that remain impacted after the bone graft at the cleft side, a frequency approximately 10 times higher when compared to general population[2-7].

In patients without oral clefts, the ectopic eruption of maxillary canines (Mx.C) can be early diagnosed during the late mixed dentition using clinical exams associated to panoramic radiograph images. Ericson and Kurol[1a] suggested that (1) asymmetry on canine bud palpation between two sides, (2) inability to palpate the canine and (3) maxillary lateral incisor (Mx.L2) late eruption or pronounced buccal or labial displacement are clinical signs of maxillary canine eruption disturbance. In the panoramic radiograph, the superimposition of the cusp tip of maxillary canine buds with the root of the lateral or central incisors is a sensible method to predict canine impaction[8,9]. This method could identify almost 80% of the canines likely to become impacted[9]. Currently studies demonstrate that an increased mesiodistal inclination of

permanent canine after autogenous bone graft seems to be associated to canine impaction in CLP[4,5,7].

Canine impaction in non-cleft (NC) patients is related to a genetic background[10-15] and is associated with other dental anomalies as tooth agenesis and small teeth[10,13,16]. However, factors that can contribute for a higher prevalence of impacted canines in unilateral cleft lip and palate (UCLP) are still unknown. Some authors associate impacted canines and the lack of bone in alveolar defect, which can reduce the available space in the jaw and result in canine displacement[5]. Indeed, bone graft surgery[17] and timing[4] to repair the cleft could interfere in permanent canine eruption. Additionally, it has been suggested a positive relation between tooth agenesis, clefting and genetic disturbances[18]. May impacted canines in UCLP patients share the same genetic etiology as dental anomalies? Or canines remain impacted as a consequence of the cleft environment? These questions still do not have evidence-based answers and we still need a trustable method for early detection of canine impaction in CLP.

Considering the benefits of prevention to reduce the burden of care in patients with CLP, this study has three objectives: (1) to longitudinally assess permanent canine eruption path in the recombinant human Bone Morphogenetic Protein (rh-BMP2) grafted alveolar cleft compared to antimere tooth at non-cleft side; (2) to evaluate early risk indicators of maxillary canines impaction at the cleft side and (3) to examine prevalence of dental anomalies associated with canine impaction in patients with UCLP.

Material and Methods

The study was approved by the Institutional Ethical Committee (Protocol. 17860713.5.0000.5441) of the Hospital for Rehabilitation of Craniofacial Anomalies, University of São Paulo. The sample consisted of 75 patients with complete unilateral cleft lip and palate who underwent secondary alveolar bone grafting with rhBMP-2 (mean age of 9.8±0.7 years) at a single center. The inclusion criteria were: consecutive patients that performed secondary alveolar bone grafting (SABG) from 2009-2014 with rhBMP2 (Infusion®); presence of the complete set of panoramic radiographs before (T1), from 3 to 12 months after SABG (T2) and more than 13 months after SABG (T3). Exclusion criteria were: patients with associated craniofacial syndromes and patients

whose radiographs showed poor image quality. From 75 patients, between 90 to 100% underwent to RME before SABG. The cleft side (CS) group comprised permanent maxillary canines at the cleft side. The non-cleft side (NCS) group comprised the contralateral permanent maxillary canines at the non-cleft side. Impacted canines were recorded due to the presence of access surgery for posterior canine traction. Digital panoramic radiographs taken immediately before (T1), after 3 to 12 months of SABG (T2) and after 13 to 48 months after SABG (T3) were used. Dolphin Imaging software 10.5 (Dolphing Imaging, Charsworth, CA, USA) was used to measure the following parameters on all the radiographs: mesiodistal angulation and height of the maxillary canine buds, horizontal displacement of maxillary canine bud relative to the neighboring incisors, dental agenesis, transposition, distoangulation.

The mesiodistal angulation of the canine bud was measured using the angle formed between the long axis of the maxillary canine and the bicondylar line[19] (Figure 1). The canine bud height was measured from the cusp tip to the occlusal plane, perpendicularly (Figure 1).

A modified method based on Ericson and Kurol and Lindauer et al.[8,9] studies was used for evaluating the mesiodistal canine germ displacement relative to the roots of central and lateral incisors at the cleft and non-cleft sides, respectively (Figure 2). When maxillary lateral incisor was missing at the NCS, the measurement was performed in adjacent central incisor. However, when central incisor was missing at the CS, this method could not be performed. Only non-erupted canines were recorded between sectors 1, 2 and 3, which justify the decreased number of the sample in table 6. The classification between erupted and non-erupted canine was done according to the panoramic analisis and relative position of the canine cusp tip and occlusal plane: canines above the occlusal plane (distance < 0) were considered as non-erupted and canines under the occlusal plane (distance ≥ 0) were considered as erupted.

Dental agenesis, excluding third molar, distoangulation of second premolars and tooth transpositions were assessed by direct observation of each panoramic radiographs. Distoangulation of lower second premolar was performed according to the method described by Shalish et al[20] using the mandible lower border as a reference line.

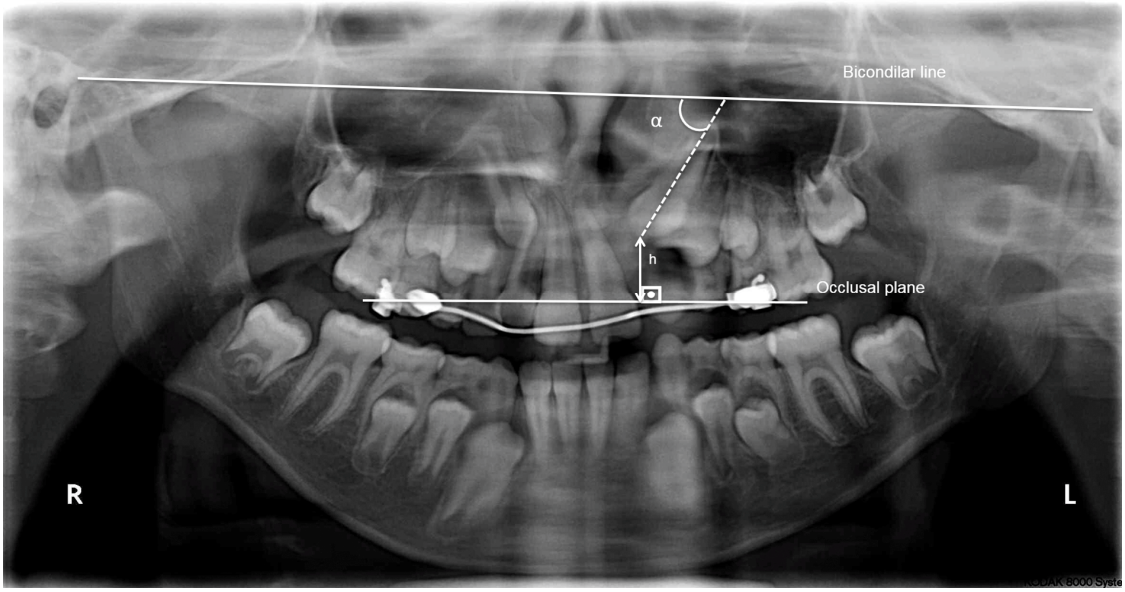

Figure 1: The bicondilar line passing through the superior region of the condyles[19] was used as reference for measuring mesiodistal angulation of maxillary canines (α). Maxillary canines height were measured relative to the occlusal plane passing though the mesiobuccal cusp tip of maxillary permanent first molars (h)**.** As alpha decreases, canine mesiodistal angulation increases.

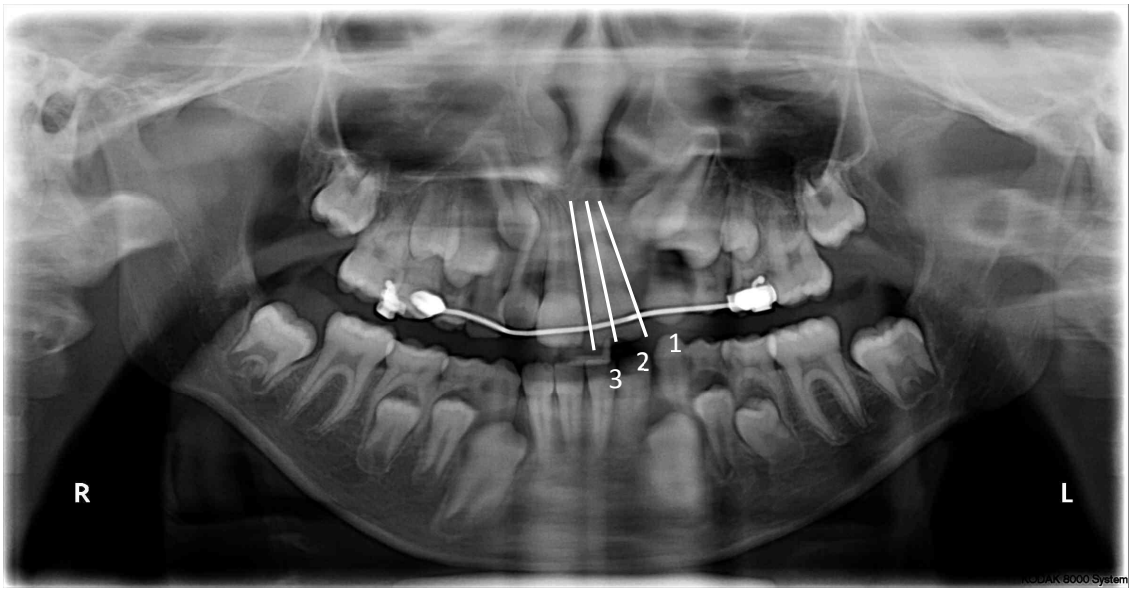

Figure 2: Mesiodistal displacement of maxillary canines buds were scored following the position of cusp tip into the three sectors of the neighboring incisor. At the non-cleft side, the maxillary lateral incisor root was used as reference [8,9]. At the cleft side, due the high prevalence of absent and small lateral incisors, only the central incisor root was used as reference.

Two examiners performed the measurements twice with an interval of 30 days. Intraexaminer and interexaminer reliability was calculated using the intraclass correlation coefficient (ICC) and Kappa test. The average and standard deviation of the assessed quantitative parameters were calculated. Interphase differences for maxillary canine position were evaluated using ANOVA. Prevalence of impaction and dental anomalies were calculated in percentage. Comparisons of canine positional parameters between cleft and non-cleft sides and between impaction and non-impaction cases were performed respectively using paired and independent t-tests. Comparisons for the frequency of associated dental anomalies between impaction and non-impaction cases were performed using Fisher test. Comparison of the horizontal position of the canines (sectors) between clef and non-cleft sides and between impacted and non-impacted canines was performed using Fisher test. Specificity and sensitivity tests were performed for the cleft side canine angulation at T1. The significance level regarded was 5%. Statistical analysis was developed with the assistance of SPPS software (version 16.0, SPPSS, Chicago, IL, USA) for the Windows operating system.

Results

The intraexaminer and interexaminer reliability for the variables ranged from 0.85 to 0.97 and 0.73 to 0.97, respectively. For Kappa intraexaminer reliability was around 0.8 and interexaminer reliability were and 0.58 to 0.76, only for sectors (Table 1).

The study sample consisted of 75 consecutive patients with non-syndromic UCLP (32.9% females and 67.1% males). The ratio between the left and right side cleft was approximately 2:1. At the CS, 18 (24%) individuals showed impacted canine and 57 had fully erupted canine (76%). At the non-cleft side, 1 (1.3%) canine was impacted.

From T1 to T3, the height and mesiodistal angulation of the maxillary canines decreased both at the cleft and non-cleft sides (Table 2).

At the three time points, the cleft side demonstrated maxillary canines more angulated and more distant from the occlusal plane (Table 3).

Table 4 shows that individuals who maxillary impacted canines become impacted at the cleft side demonstrated an increased mesiodistal angulation and

height since the pre bone graft stage. Angulations higher than 68.6° pre bone graft at CS are likely to became impacted.

The mesiodistal position of the canine bud at the cleft side (sectors) was not a discriminant factor between impacted and non-impacted canines (Table 5).

Mx.L2 agenesis at the CS was the only parameter that presented statistically significantly difference, although Mx.L2 agenesis at NCS and tooth transposition presented a higher rate on the impacted canine group (Table 6).

Table 1- Intra and interexaminer reproducibility (Intraclass Correlation Coefficient and Kappa test).

		Intra-examiner	Inter-examiner
	Variables	ICC	ICC
CS	Angulation	0.97	0.95
	Height	0.97	0.97
NCS	Angulation	0.94	0.96
	Height	0.93	0.93
		Kappa	Kappa
CS	Mesiodistal sectors	0.80	0.58
NCS	Mesiodistal sectors	0.81	0.76

CS, cleft side; NCS, non-cleft side

Table 2- Canine position at the cleft and non-cleft sides in the three timepoints (ANOVA test).

	T1		T2		T3		
	Mean	SD	Mean	SD	Mean	SD	p
CS							
Angulation (α)	67,85[a]	14.23	65.62[a]	15.47	74.42[b]	16.09	0.000
Height (h)	-11.58[a]	5.30	-7.05[b]	6.55	-1.67[c]	7.51	0.000
NCS							
Angulation (α)	79.48[a]	12.15	82.63[b]	11.59	86.62[c]	8.33	0.000
Height (h)	-7.74[a]	6.37	-2.63[b]	6.84	1.92[c]	5.89	0.000

CS, cleft side; NCS, non-cleft side

Table 3- Comparison between cleft (CS) and non-cleft side (NCS) for quantitative parameters (paired t test).

	CS		NCS			
	Mean	SD	Mean	SD	Dif	p
Angulation (α) T1	67.85	14.23	79.48	12.15	-11.63	0.000
Height (h) T1	-11.58	5.30	-7.74	6.37	-3.84	0.000
Angulation (α) T2	65.62	15.47	82.63	11.59	-17.01	0.000
Height (h) T2	-7.05	6.55	-2.64	6.84	-4.42	0.000
Angulation (α) T3	74.42	16.09	86.62	8.33	-12.20	0.000
Height (h) T3	-1.67	7.51	1.92	5.89	-3.59	0.000

CS, cleft side; NCS, non-cleft side

Table 4- Comparison between impacted and non-impacted canines at the cleft side (Independent t-tests).

	Impacted canines		Non-impacted canines		
	Mean	SD	Mean	SD	p
Angulation (α) T1	56.98	14.33	71.28	12.45	0.000
Height (h) T1	-14.46	4.90	-10.66	5.12	0.007
Angulation (α) T2	53.22	14.60	69.53	13.66	0.000
Height (h) T2	- 11.46	6.20	-5.65	6.06	0.002
Angulation (α) T3	62.24	18.46	78.26	13.26	0.000
Height (h) T3	-7.10	9.11	0.04	6.06	0.000

Table 5- Mesiodistal sectors comparison between impacted and non-impacted canines at the cleft side (Fisher test).

Pre bone graft T1				
	Sector 1	Sector 2	Sector 3	p
Impacted	88,9% (n=16)	11.1% (n=2)	0.0 % (n= 0)	0.247
Non-impacted	96.4% (n=54)	3.6% (n=2)	0.0% (n=0)	
3-12 months post bone graft T2				
	Sector 1	Sector 2	Sector 3	p
Impacted	81.3% (n=13)	6.2% (n=1)	12.5 % (n= 2)	0.085
Non-impacted	87.5% (n=42)	12.5% (n=6)	0.0% (n=0)	
13-48 months post bone graft T3				
	Sector 1	Sector 2	Sector 3	p
Impacted	53.8% (n=7)	38.5% (n=5)	7.7 % (n= 1)	0.052
Non-impacted	85.2% (n=23)	14.8% (n=4)	0.0% (n=0)	

Table 6- Comparison of the frequency of dental anomalies in subjects with and without canine impaction (Fisher test).

	Impacted canines %	Non-impacted canines %	p
Tooth Agenesis	16.6	22.8%	0.747
Mx.L2 agenesis NCS	16.6%	8.7%	0.389
Mx.L2 agenesis CS	72.2%	33.3%	0.006
Md.P2 distoangulation	0%	8.7%	0.329
PM agenesis	0.0%	14.0%	0.186
Tooth Transposition	5.5%	3.6%	0.999

CS, cleft side; NCS, non-cleft side; Mx.L2, maxillary lateral incisor; Md.P2, mandibular second premolar; PM, premolar

Discussion

Studies have described predictor factors for permanent canine impaction over the years [3-7,21]. In the present study, mesiodistal angulation, distance from the occlusal plane, mesiodistal displacement and associated dental anomalies were investigated as possible risk indicators for canine impaction in UCLP. The prevalence of canine impaction was 24% at the cleft side (CS) corroborating previous studies that showed a prevalence ranging from 12 to 35% of canine impaction in CLP[2-7]. At the non-cleft side, the prevalence rate of canine impaction was 1.3%. A previous study reported a prevalence of 2.9%[7]. The possible explanations for the much higher prevalence of canine impaction adjacent to the alveolar cleft could be the lack of bone in the cleft area as well as the graft surgery to repair the alveolar defect[17] and SABG timing[4].

The methodology used for angulation measurements was based on Parenti et al[19] previous study. Internal angle between canine long axis and the bicondilar line showed an adequate reliability and reproducibility due to the facility of recognizing the most superior points of the condyles in the panoramic radiographs[19,22]. In patients with CLP, adopting dental midline as a reference line for canine angulation measurement

would not be possible because dental midline is normally deviated. Additionally, the permanent maxillary central incisor at the cleft side is usually rotated which makes the localization of the midline even more difficult. The occlusal plane was previously reported as a reference for measuring height of impacted canines in non-cleft patients[8,23] and was reported as an earlier predictor factor of impaction in non-cleft patients[23]. In previous studies, the occlusal plane was usually traced from the incisal edge of the central permanent incisor to the first permanent molar at the same side in non-cleft individuals[23]. In contrast, our study used a line traced between the mesial cusps of the permanent maxillary first molars as an occlusal plane since maxillary central incisors at the CS are usually rotated and malpositioned. This methodology showed an excellent inter and intraexaminer reability (Table 1).

Our results revealed that besides canines at the CS were more angulated and more distant from the occlusal plane when compared to non-cleft one, both decreased angulation and height from T1 to T3. Canines became more vertical and closer to the occlusal plane, corroborating with previous results[4,6]. Bone graft before permanent canine eruption usually allows the spontaneous migration and eruption of the adjacent maxillary canine[6,21,24]. However, some authors reported no change in canine angulation after SABG[25]. When impacted and non-impacted canine were compared, impacted canines agreed with previous studies and presented an increased mesiodistal angulation[4,5,7] and height and it might be a predictable feature for impaction in UCLP. It is also true for non-cleft patients, which impacted canines were observed more distantly from the occlusal plane when compared with its antimere[8,23].

The most widely used and reliable method for predicting canine impaction in non-cleft individuals used maxillary incisor sectors as a positional parameter for impaction predictor[8,9]. However, it has been suggested that sectors are not applicable in UCLP patients because the lateral incisor is frequent missing[22]. This study described a method using sectors as predictor factor for UCLP patients. Differently from Russel an McLeod[4] previous study, the maxillary central incisor was used as a reference at the CS because the Mx.L2 is usually anomalous in the cleft area and present a variation in number and location. The results showed that the minority of the impacted canines at the CS showed any overlapping to the adjacent central incisor at T1 (Table 5). In other words, the maxillary canines which become impacted at the cleft side were positioned distally to maxillary central incisors before SABG probably because the presence of the alveolar cleft. This finding agrees with Russel and McLeod[4] that

suggested a fewer laterally movement prior SABG in consequence of the erupting canine located distal to the cleft site. After the bone graft procedure (T2), an increased number of canines was observed at sectors 2 and 3 both in impacted and non-impacted subgroups. At T3, the majority of impacted canines were still lying distal to adjacent central incisors (Table 5). In the light of these results, the mesiodistal position of canine buds can not be considered an early risk factor for impaction at the cleft side in patients with UCLP.

Prevalence of dental anomalies with genetic background was investigated in the impacted and non-impacted canines subgroups. No differences were observed between groups except for the agenesis of maxillary lateral incisors at the cleft side that was more prevalent in the individuals with CS canine impaction (Table 6). Studies have reported a correlation between impacted canine and missing lateral incisor[2,4,26], suggesting that the presence of lateral incisor may guide the eruption of the canine through the grafted area, whereas some authors have not[5-7,25]. In this regard, the agenesis of maxillary lateral incisors at the cleft area may constitute a risk indicator for canine impaction.

Our results have identified that an increased mesidiostal inclination ($\leq 68.6°$) and the agenesis of maxillary lateral incisors at the cleft side constitute early risk factor for canine impaction in UCLP. Future studies should investigate possible preventive procedures for avoiding canine impaction in UCLP. An increased mesiodistal angulation and height from the occlusal plane, as well as maxillary lateral incisor agenesis at CS seems to be risk indicators for canine impaction in UCLP. However, this study could not clearly distinguish the role of genetics and environment in the etiology of maxillary canines at the cleft region. The higher prevalence of impaction at the cleft side compared to the non-cleft side as well as the increased frequency of agenesis of the neighboring maxillary lateral incisor point to a local or environmental background for canine impaction in UCLP. On the other hand, an increased mesiodistal angulation since the pre bone graft stage points that the genetic background can also be an important factor.

Conclusion

Impacted canines at the CS in UCLP showed an increased mesial angulation and an increased height from the occlusal plane since pre bone graft phase. Associated with maxillary lateral incisor agenesis at CS, these findings seem to be risk indicators for canine impaction in UCLP. However, the mesial displacement and superimposition with neighboring incisors should not be used as predictor factors for canine impaction in UCLP. This study could not elucidate the role of genetics and environment in the etiology of maxillary canines at the cleft region.

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4 CONCLUSION

4 CONCLUSION

Impacted canines at the CS in UCLP showed an increased mesial angulation and an increased height from the occlusal plane since pre bone graft phase. The mesial displacement and superimposition with neighboring incisors did not predict canines likely to become impacted and should not be used as predictor factors for canine impaction in UCLP.

An increased mesial angulation and height from the occlusal plane, whereas associated with Mx.L2 agenesis at CS seems to be a risk indicator for impaction in UCLP. However, this study could not discern between genetic or environmental cause for maxillary canine impaction and further studies may be needed.

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