Maurício Augusto Aquino de Castro

AVALIAÇÃO DA OCORRÊNCIA DE RAMIFICAÇÕES DOS CANAIS MANDIBULARES EM REGIÕES AFETADAS OU NÃO POR INFLAMAÇÃO POR MEIO DE TOMOGRAFIA COMPUTADORIZADA DE FEIXE CÔNICO

Belo Horizonte

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Tese apresentada ao Programa de Pós-Graduação em Odontologia da Faculdade de Odontologia da Universidade Federal de Minas Gerais como requisito parcial para a obtenção do título de Doutor em Odontologia.

Área de Concentração: Estomatologia

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EPÍGRAFE

“Um pouco de ciência nos afasta de Deus.

Muito, nos aproxima.”

Louis Pasteur

RESUMO

O canal mandibular precisa ser considerado em diversos procedimentos odontológicos, com vistas a evitar injúrias do nervo alveolar inferior. A ocorrência de variações anatômicas do canal mandibular aumenta o risco de lesões neurovasculares. Sensibilidade aumentada e falhas em procedimentos anestésicos em mandíbulas, especialmente em casos com inflamação, também podem estar relacionadas com alterações da inervação local. Este estudo visou avaliar a ocorrência de ramificações dos canais mandibulares em regiões afetadas por inflamação dentária, por meio de tomografia computadorizada de feixe cônico (TCFC), com o intuito de verificar se há algum relacionamento entre ramificações e inflamação. Uma base de dados de 2.484 TCFCs foi revisada para identificar ramificações dos canais mandibulares e inflamação dentária. A amostra final foi pareada para idade e gênero. As ramificações próximas aos dentes posteriores foram consideradas como variável dependente. A ocorrência e localização de inflamação dentária, assim como as medidas dos níveis de cinza nas mesmas regiões, foram consideradas como variáveis independentes. Os testes de Kolmogorov-Smirnov, Qui-quadrado, teste-T e análise por regressão logística foram aplicados para verificar o relacionamento estatístico dos dados (P<0,05). As lesões mais relacionadas às ramificações foram lesões endoperio e lesões apicais. Gênero (P=0,308) e idade (P=0,728) não mostraram associação com a ocorrência de ramificações dos canais mandibulares. A ocorrência de inflamação aumentou o risco para a ocorrência de ramificações dos canais mandibulares próximas aos dentes posteriores. (P<0,001; OR=11,640; IC-95%: 4.327-31.311). As lesões mais frequentemente associadas com as ramificações apresentaram origem endodôntica. Foi verificada associação entre as ramificações dos canais mandibulares e inflamação dentária na região dos dentes posteriores.

Palavras-chave: Mandíbula. Nervo alveolar inferior. Canal mandibular. Canal mandibular bífido. Tomografia computadorizada de feixe cônico.

ABSTRACT

Mandibular canal branching and dental inflammation assessed through cone beam computed tomography

The mandibular canal must be considered in several dental procedures in order to avoid injuries of the alveolar inferior nerve. The occurrence of anatomical variations of the mandibular canal increases the risk of neurovascular injuries. An increased sensitivity and failed anesthetic procedures in mandibles, especially in cases with inflammation, can be also related with alterations of the local innervation. This study aimed to assess the occurrence of mandibular canal branching (MCB) in alveolar ridges affected by dental inflammation by means of cone beam computed tomography (CBCT), in order to verify if there is some relationship between MCB and dental inflammation. A database of 2,484 CBCTs was reviewed for identifying mandibular canal branching (MCB) and dental inflammation in mandibular alveolar ridges. The final sample was matched by age and gender. MCB nearby the posterior teeth was considered as the dependent variable. Dental inflammation occurrence and location as well as measurements of gray levels at the same region were assessed as independent variables. The Kolmogorov-Smirnov, Chi-square, T-test and multiple logistic regression analysis were applied to verify the statistical relationship of the data ($P<0.05$). The most frequent inflammatory lesion was apical radiolucency with endodontic origin. The lesions mostly related to MCB were combined endodontic and periodontal lesions and apical lesions. Gender had no influence on mandibular canal branching ($P=0.308$), not did age ($P=0.728$). The occurrence of dental inflammation increased the risk for occurrence of the MCB nearby posterior teeth ($P<0.001$; OR=11.640; CI-95% 4.327-31.311). The gray levels had a minor role on the presence of MCB ($P=0.002$; OR=1.002; CI95% 1.002-1.003). The lesions most often associated with the branches had endodontic origin. An association between MCB situated around the posterior teeth and dental inflammation was found.

Key Words: Mandible; inferior alveolar nerve; mandibular canal; bifid mandibular canal; cone beam computed tomography.

LISTA DE TABELAS

LISTA DE SIGLAS E ABREVIATURAS

TCFC – Tomografia computadorizada de feixe cônico

RCM – Ramificação do canal mandibular

mm – Milímetros

FOV – do inglês, f*ield of View* (Campo de visão)

cm – Centímetros

ROI – do inglês, *region of Interest* (Região de Interesse)

CM – Canal mandibular

CBCT – do inglês, c*one beam computed tomography* (tomografia computadorizada de feixe cônico.

MCB – do inglês, m*andibular canal branching* (ramificação do canal mandibular)

LED – do inglês, *light emission diode* (emissão de luz por diodo)

SUMÁRIO

1 - Introdução

O feixe neurovascular alveolar inferior é uma importante estrutura anatômica a ser considerada em odontologia. O feixe adentra o canal mandibular, um ducto intraósseo usualmente único em cada hemi-mandíbula, sendo o principal responsável pela inervação e suprimento sanguíneo das estruturas mandibulares. (Carter & Keen, 1971; Nortjé et al., 1977[1]; Langlais et al., 1985; Kieser et al., 2005; Rodella et al., 2012).

Ramificações neurovasculares da região mandibular são variações morfológicas da normalidade e podem ocorrer com o nervo alveolar inferior ou com o nervo milohióideo (Durst & Snow, 1980; Bennett & Towsend, 2001; Rodella et al., 2012). É necessário conhecer a anatomia do canal mandibular, à fim de se evitar lesões do nervo alveolar inferior, hemorragias ou distúrbios de sensibilidade, (Claeys & Wackens, 2005; Rouas et al., 2007; Kuribayashi et al., 2010; Kim et al. (2010); Mizbah et al., 2012; Muinelo-Lorenzo e al., 2014; Kang et al., 2014).

Variações morfológicas dos canais mandibulares são supostamente relacionadas com má-formações embrionárias derivadas de falha na fusão de canais ósseos primitivos no período pré-natal (Chávez-Lomelí et al, 1996). Há também relatos de alterações dos canais mandibulares, tais como ausência, alargamento do canal e crescimento de massa ligada ao canal, congênitas ou associadas com alterações pós-natais (Jakobsen et al., 1991; Buric et al, 2010; Manikandhan et al., 2010; Sheik et al, 2010).

Estudos têm relatado não haver diferenças em relação ao gênero ou à idade para a ocorrência de ramificações dos canais mandibulares (RCM) (Salvador et al., 2010; Kang et al., 2014; Oliveira-Santos et al., 2012; Orhan et al., 2013). Fu et al. (2014) e Muinelo-Lorenzo et al. (2014) encontraram associação estatisticamente significativa da ocorrência de canais bífidos em homens.

A prevalência das RCM variam de acordo com o tipo de teste diagnóstico usado. Exames radiográficos bidimensionais foram o principal recurso diagnóstico para a identificação do trajeto dos canais mandibulares, mesmo com limitações inerentes a esse tipo de exame (Carter & Keen, 1971; Chávez-Lomelí et al, 1996;

Nortjé et al., 1977[1,2], Langlais et al., 1985). Em radiografias panorâmicas, as ramificações foram localizadas principalmente na região dos ramos mandibulares, com prevalência variando de 0,08% a 16,8% (Durst & Snow, 1980; Grover & Lorton, 1983; Nortjé et al., 1977[1]; Langlais et al., 1985; Muinelo-Lorenzo et al., 2014). Kim et al. (2010) demonstraram que radiografias panorâmicas não apresentam satisfatória especificidade na identificação de RCM. Embora Mizbah et al. (2012) tenham considerado os exames bidimensionais como tendo uma boa acurácia diagnóstica, estudos mostram não haver concordância entre os exames panorâmicos e tomografias computadorizadas (Muinelo-Lorenzo et al, 2014; Sanchis et al., 2003).

Para superar essas limitações, os exames tridimensionais (3D) permitiram melhorias na identificação da morfologia dos canais mandibulares, conferindo maior acurácia, comparativamente a outros métodos de diagnóstico por imagem (Miller et al., 1990; Sanchis et al., 2003; Claeys & Wakens, 2005; Rouas et al., 2007; Naitoh et al., 2009; Kim et al., 2010; Neves et al., 2010; Kuribayashi et al., 2010; Rodella et al., 2012; Fukami et al., 2012; Muinelo-Lorenzo et al., 2014). Nos exames 3D, as RCM também foram encontradas primordialmente nas regiões dos ramos, porém com maior prevalência (9,8% a 65%) (Sanchis et al., 2003; Claeys & Wackens, 2005; Rouas et al., 2007; Naitoh et al., 2009; Kuribayashi et al., 2010; Neves et al., 2010; Rodella et al., 2012; Muinelo-Lorenzo et al., 2014; Kang et al., 2014, Fu et al., 2014).

De acordo com a suposição de Langlais et al. (1985), novas variações dos canais mandibulares, sem classificação adequada na literatura, têm sido relatadas (Mader & Konzelman, 1981; Wadhwani et al., 2008). Melhorias promovidas com os exames 3D aumentam ainda mais as chances para a detecção de novas variações (Claeys & Wakens, 2005, Rouas et al., 2007; Manikandhan et al., 2010).

O grande número de procedimentos executados na região posterior de mandíbulas implica que a identificação dos canais mandibulares necessita de especial atenção dos clínicos. Há relatos de considerável dor pós-operatória devido a injúrias do nervo alveolar inferior (Juodzbalys et al., 2011; Siqueira & Siqueira, 2011).

Uma vez que avaliações histológicas comprovaram a presença de ramos do nervo alveolar inferior no interior de RCM (Ikeda et al., 1996; Fukami et al., 2012), a ocorrência destas variações morfológicas aumenta o risco de danos neurovasculares e alterações sensitivas em mandíbulas (Juodzbalys et al., 2011). Deste modo, as RCM precisam ser consideradas nos planejamentos de procedimentos cirúrgicos para inserções de implantes, extrações de dentes inclusos, realização de biópsias ou enucleação de patologias, assim como em intervenções cirúrgicas apicais, osteotomias sagitais, realização de enxertos ósseos e em procedimentos anestésicos (Grover & Lorton, 1983; Langlais et al., 1985; Hori et al., 2001; Sanchis et al., 2003; González-Santana et al., 2005; Kieser et al., 2005; Rouas et al., 2007; Simonton et al., 2009; Naitoh et al., 2009; Kim et al., 2010; Judozbalys et al., 2010; Kuribayashi et al., 2010; Neves et al., 2010; Juodzbalys et al., 2011; Siqueira & Siqueira, 2011; Mizbah et al., 2012; Oliveira-Santos et al., 2012; Orhan et al., 2013; Kang et al., 2014).

Chama a atenção o aumento da sensibilidade dolorosa e dificuldades com procedimentos anestésicos em regiões afetadas por inflamação, notadamente em mandíbulas. Além da ação de fatores álgicos relacionados à inflamação, uma hipótese é referida à ocorrência de variações anatômicas dos nervos responsáveis pela sensibilidade em mandíbulas (Najjar, 1977; Walton & Abott., 1981; Wallace et al., 1985; Cohen et al., 1993; Potocnic & Bajrovic., 1999; Blanton & Jeske, 2003).

Interação entre inflamação e alteração nervosa foi identificada mesmo quando o local da inflamação estava relativamente distante da alteração neurovascular (Najjar, 1977). Regeneração de raízes dorsais da medula de cobaias e neurogênese em discos intervertebrais humanos já foram observadas e relacionadas com a ação de mediadores inflamatórios (Di Maio et al., 2011; Lee et al., 2011). Ainda assim, os fenômenos biológicos envolvidos nestas situações não estão esclarecidos, não sendo possível determinar o verdadeiro papel da inflamação em relação à inervação suplementar nestas situações (Najjar, 1977; Wallace et al., 1985; Potocnic & Bajrovic, 1999).

Achados de RCM direcionadas para lesões inflamatórias dentárias, detectados pelos pesquisadores da presente tese, corroboram com a suspeita de que possa haver alguma associação entre inflamação e RCM. A proposta deste estudo foi avaliar as RCM situadas nos processos alveolares afetados por lesões inflamatórias, usando uma grande amostra de tomografias computadorizadas de feixe cônico (TCFC), obtidas em dois diferentes centros de radiologia odontológica, no Brasil e no Canadá.

Se verificada alguma associação entre estas alterações, essa terá relevante significado clínico por contribuir para a previsibilidade da localização das RCM e para explicar o insucesso de procedimentos anestésicos em mandíbulas com lesões inflamatórias. Além disso, os achados poderão estimular novos estudos sobre os fatores inflamatórios envolvidos em tal resposta neurovascular, podendo ser a base de um futuro tratamento de lesões neurovasculares em odontologia.

2 - Revisão de Literatura

2.1 - Relevância clínica da detecção do canal mandibular e suas variações

A identificação e localização dos canais mandibulares tem grande importância e merece atenção por parte dos clínicos, devido ao risco de acidentes durante procedimentos cirúrgicos em mandíbulas, que possam resultar em lesão do feixe neurovascular alveolar inferior, o principal responsável pela inervação e suprimento sanguíneo das estruturas mandibulares. A ocorrência de variações dos canais mandibulares aumenta consideravelmente o risco de dano neurovascular, devido a menor previsibilidade da localização das estruturas neurovasculares. (Durst & Snow, 1980; Hori et al., 2001; González-Santana et al., 2005; Simonton et al., 2009; Kim et al., 2010; Mizbah et al., 2012)

Robert et al. (2005) entrevistaram 535 cirurgiões bucomaxilofaciais sobre a ocorrência de acidentes com lesões nervosas, ocorridas durante procedimentos para remoção de terceiros molares inferiores. 94,5% dos cirurgiões relataram acidentes envolvendo o nervo alveolar inferior e 53% relataram acidentes com o nervo lingual, em um período de 12 meses. 78% dos cirurgiões relataram que houve injúrias permanentes do nervo alveolar inferior, ao longo de sua vida profissional. As taxas relatadas de lesões do nervo alveolar inferior foram em torno de 4 à cada 1000 extrações e de 1 à cada 1000 extrações nos casos de lesões do nervo lingual. Enquanto as causas de lesões do nervo alveolar inferior foram conhecidas, para o nervo lingual os cirurgiões relataram não conhecer as causas.

Tay **&** Zuniga (2007) avaliaram as características clínicas de injúrias nervosas decorrentes de procedimentos odontológicos. Os autores verificaram que o nervo alveolar inferior foi o mais comumente lesado, com 64% das lesões. As etiologias mais comuns incluíram cirurgia para remoção de terceiros molares (52%), injeções anestésicas locais (12%), cirurgia ortognática (12,3%) e inserções de implantes (11%). Das lesões ocorridas devido à inserção de implantes, 14,9% dos pacientes desenvolveram dor neuropática ao longo do tempo, com pouca ou nenhuma recuperação nervosa.

Após avaliação de 449 casos com lesões iatrogênicas em mandíbulas, Hillerup (2007) detectou que o nervo lingual foi o mais afetado (58,1%), seguido pelo nervo alveolar inferior (33,2%). Os procedimentos que mais comumente ocasionaram as lesões foram remoções de terceiros molares (71%), injeções anestésicas (17,4%), inserções de implantes (3,6%) e tratamentos endodônticos (2,2%). A parestesia foi a consequência mais comumente relatada (53,5%), seguida por disestesia (17,7%) e alodinia (4,5%).

Aprofundando sua avaliação, Hillerup (2008) avaliou longitudinalmente a evolução de 52 pacientes com histórico de lesões iatrogênicas unilaterais do nervo alveolar inferior. Dentre estes pacientes, as cirurgias de remoção de terceiros molares corresponderam a 69% dos casos, as lesões por injeções anestésicas responderam por 10% e as inserções de implantes foram responsáveis por 10% das lesões. As injúrias decorrentes de exodontias de terceiros molares apresentaram significativa recuperação ($p<0,001$), enquanto as demais etiologias não apresentaram recuperação. Um dos casos de lesão por inserção de implantes apresentou marcada piora, com perda total de percepção sensorial, comparando-se a avaliação inicial e final.

Em revisão de literatura sobre sensibilidade dolorosa pós-operatória em implantodontia, Siqueira & Siqueira (2011) relatam que queixas de alterações de sensibilidade após intervenções cirúrgicas geram dúvidas, pois nem sempre há relação clara entre implante e o nervo alveolar inferior. Os estudos existentes sobre o tema normalmente consideram questões relacionadas à osteointegração, sendo raros os estudos que avaliam perdas relacionadas à lesão de nervo ou à dor neuropática, mesmo considerando que o risco para a longevidade de implantes é multifatorial. Os autores ressaltam que, em conjunto, essas informações poderiam contribuir para a adoção de conduta que inclua minucioso exame pré-operatório, exames interconsultas, medidas preventivas, curativas ou paliativas para o tratamento da dor e ações diagnósticas especializadas, incluindo os exames de imagem.

Juodzbalys et al (2011) revisaram estudos que relataram prevalências de até 40% de alterações da percepção sensorial após a inserção de implantes, impondo sérios problema relativos à qualidade de vida dos pacientes

Além dos riscos inerentes de lesão neurovascular durante procedimentos cirúrgicos, há dificuldades com a efetividade de procedimentos anestésicos em dentes inferiores que também podem estar relacionadas com variações morfológicas do nervo alveolar inferior. Tais variações, representadas por ramificações dos canais mandibulares, presença de forames mentuais adicionais e variações do nervo milohióideo, são consideradas como potenciais causas de falhas de procedimentos anestésicos (Najjar, 1977; Grover & Lorton, 1983; Bennet & Towsend, 2001; Blanton & Jeske, 2003).

Cohen et al., (1993) também constatou dificuldade para a efetivação de anestesia em molares inferiores, notadamente quando em presença de inflamação. O pesquisador verificou que a sensação de anestesia no lábio inferior não é um adequado critério para verificar a efetivação da anestesia de dentes com inflamação, que podem permanecer sensíveis e necessitarem de anestesia intraligamentar complementar para a continuidade dos procedimentos.

Apesar da ocorrência de inflamação representar uma situação clínica de conhecida dificuldade para o êxito de anestesia, não é certo considerar que a inflamação seja a única razão para as falhas dos procedimentos anestésicos. Como os dentes inferiores inflamados são menos susceptíveis à anestesia, comparativamente aos dentes superiores, as variações anatômicas nervosas são consideradas como possível causa dessa alteração (Walton & Abott, 1981; Potocnic & Bajrovic, 1999).

O procedimento cirúrgico de instalação de implantes posteriores ao forame mentual em rebordos reabsorvidos é considerado como sendo de difícil execução devido à proximidade do canal mandibular e, consequentemente, ao risco de lesão do nervo alveolar inferior (NAI). Uma vez que há relatos de considerável dor pós-operatória de origem neuropática decorrente de injúria do canal mandibular, esse reparo anatômico precisa ser considerado nos planos de tratamento cirúrgicos, como os de inserção de implantes, remoção de dentes inclusos, cirurgias apicais, osteotomias sagitais e biópsias, incluindo a abordagem anestésica (Siqueira & Siqueira, 2011).

2.2 - Etiologia das ramificações dos canais mandibulares

Com base na análise de radiografias laterais de 302 hemimandíbulas fetais encontradas em escavações arqueológicas, Chávez-Lomelí et al. (1996) teorizaram que a formação destas alterações se daria em período embrionário. Os pesquisadores introduziram cones de guta percha em foraminas situadas nas superfícies linguais dos ramos mandibulares e observaram que a maioria dos cones era conduzida anteriormente em três ou mais canais. Desse modo, deduziu-se que as variações dos canais mandibulares se originam por falha na fusão de canais embrionários, que teoricamente se fundiriam e formariam forame mandibular e canal mandibular únicos em cada hemimandíbula.

Relatos de algumas variações anatômicas dos canais mandibulares sugerem que estas alterações podem estar associadas com outros fatores. O caso de uma paciente de 20 anos, portadora de microsomia hemifacial no lado esquerdo, apresentado por Manikandhan et al. (2009), ilustra que a variabilidade anatômica do nervo alveolar inferior pode ser congênita, relacionada com alteração genética. O exame panorâmico mostrou ausência do canal mandibular e do forame mentual do lado afetado, com ocorrência de uma proeminente imagem radiolúcida no corpo mandibular esquerdo. Uma série de imagens tridimensionais de tomografia computadorizada demonstrou que a entrada e saída do nervo alveolar inferior eram próximas, entrando por lingual e emergindo por vestibular no ramo mandibular do lado afetado. Esta situação foi confirmada por estereolitografia e durante cirurgia ortognática para correção da deformidade. Os autores ressaltaram que a presença do nervo é considerada um pré-requisito embriológico para a indução da osteogênese local, resultando na formação do forame mandibular e do canal mandibular. No período embrionário, o nervo é interiorizado, acompanhando o desenvolvimento mandibular a partir da cartilagem de Meckel. Porém, a descrição completa do mecanismo fisiológico que explique cientificamente a ocorrência das variações anatômicas dos canais mandibulares ainda não foi encontrada na literatura.

Liang et al. (2009) realizaram estudo morfológico comparativo de mandíbulas oriundas de diferentes regiões geográficas e de diferentes períodos cronológicos. Os autores realizaram exames tomográficos de 92 mandíbulas e de 68 pacientes, divididos em três grupos, sendo: 1- mandíbulas do período Neolítico; 2- mandíbulas do período medieval e 3- mandíbulas de pacientes dos séculos XIX e XX, de diferentes regiões geográficas. Nenhuma das medidas realizadas, como os tamanhos das mandíbulas e os diâmetros dos canais mandibulares, apresentou diferenças estatisticamente significativas entre os grupos.

Salvador et al (2010) avaliaram os canais mandibulares e suas variações em 915 radiografias panorâmicas, com o intuito de avaliar alguma possível associação com gênero ou etnia dos pacientes. A aplicação do teste estatístico do Qui-quadrado, com nível de significância de 5%, não encontrou diferenças estatisticamente significativas dos canais mandibulares associadas ao gênero ou etnia.

Buric et al. (2010) relataram um caso em que foram evidenciados alargamentos significativos dos canais mandibulares, dos forames mandibulares aos forames mentuais, como o sinal mais precoce de um linfoma não Hodgkin de células B, primário em mandíbula. A ocorrência primária de linfomas não-Hodgkin em mandíbulas não é comum, sendo mais frequente em ossos longos. A patologia, diagnosticada por avaliação histológica e por imunohistoquímica (com anticorpos CD20^{+} e KI 67^{+}) foi avaliada longitudinalmente, de 2008 a 2010, em exames radiográficos panorâmicos e tomográficos. O caso evoluiu para diferentes alterações osteolíticas mandibulares, mas não apresentou nenhuma alteração em outros ossos. Inicialmente, o paciente foi equivocadamente diagnosticado e tratado como um caso de periodontopatia, com administração de antibióticos de largo espectro. Os autores ressaltaram que os poucos casos relatados na literatura fazem com que os linfomas não-Hodgkins não sejam considerados no diagnóstico diferencial de alterações em mandíbulas. Porem, o achado inicial de alargamento dos canais mandibulares, em conjunto com a evolução das técnicas de diagnóstico por imagem, em especial das tomografias computadorizadas, além de levar ao diagnóstico precoce dessa alteração maligna, com adoção mais breve de terapias oncológicas adequadas, contribui para evidenciar a possibilidade de um caráter multifatorial das variações anatômicas dos canais mandibulares.

Em avaliação tomográfica da ocorrência de canais bífidos em 173 pacientes de uma população tailandesa, Fu et al. (2012) detectaram uma prevalência de 30,6%. Embora as ramificações tenham aparentado maior diâmetro nas pacientes do gênero feminino, houve associação significativa da ocorrência de canais bífidos com o gênero masculino. Também foi observada associação significativa da ocorrência das variações com mandíbulas que apresentaram secções transversais maiores, comparativamente às mandíbulas sem ramificações.

Muinelo-Lorenzo et al. (2014) também detectaram associação estatisticamente significativa da ocorrência de RCM com pacientes do gênero masculino, considerando o número total de pacientes avaliados e o número total de lados afetados.

2.3 - Classificações das ramificações do canal mandibular

O canal mandibular é um ducto intraósseo, usualmente único em cada hemi-mandíbula, responsável pela condução do feixe neurovascular alveolar inferior. Ele se inicia no forame mandibular, situado na face lingual do ramo mandibular, e segue trajeto inferior e anterior pelo ramo e corpo mandibular, até o forame mentual.(Carter & Keen, 1971; Nortjé et al., 1977[1]; Langlais et al., 1985; Kieser et al., 2005; Rodella et al., 2012)

Em busca de maior conhecimento sobre a anatomia dos canais mandibulares e de suas variações anatômicas, Carter & Keen (1971) dissecaram oito mandíbulas e avaliaram 80 radiografias laterais convencionais de mandíbulas secas. De acordo com as características observadas nas dissecações, foi proposta a seguinte classificação (Tabela 1):

- Tipo 1: Canal mandibular composto por um único canal ósseo, próximo às raízes dos molares;

- Tipo 2: Canal mandibular situado substancialmente para inferior, com alguma distância das raízes dos molares, emitindo ramos dentais emergindo do canal principal, longas, oblíquas e direcionadas aos ápices;
- Tipo 3: Canal mandibular dá origem a dois ramos, posteriormente, com o ramo superior dirigindo-se aos ápices radiculares dos dentes posteriores e o ramo inferior seguindo anteriormente.

Com base na análise de radiografias laterais de mandíbulas, os autores observaram que os canais mandibulares são simetricamente organizados nos dois lados. Os canais únicos (tipo 1) foram o aspecto mais frequentemente encontrado (49 radiografias). Evidenciando a limitação dos exames radiográficos convencionais, em 11 radiografias os pesquisadores detectaram interrupções na cortical superior dos canais, sem ser possível determinar se eram do tipo 2 ou 3. Em 20 radiografias não foi possível visualizar adequadamente os canais.

Com base em estudo retrospectivo de uma amostra de 3612 radiografias panorâmicas padronizadas de rotina, Nortjé et al. (1977)[1] propuseram nova classificação (Tabela 1), focada nas variações dos canais mandibulares originadas nas regiões dos ramos mandibulares. Exames de pacientes com histórico de fraturas e patologias na mandíbula foram descartados, pela possibilidade de influírem na anatomia e situação dos canais. As variações encontradas foram:

- Tipo 1: Dois canais originados de um único forame mandibular. Em alguns casos os dois canais apresentam dimensões similares; mas em algumas situações o canal inferior é mais estreito;
- Tipo 2: Dois canais originados de um único forame mandibular, sendo o inferior mais longo e o canal superior curto, dirigindo-se à região dos terceiros ou segundos molares;
- Tipo 3: Dois canais de iguais dimensões, aparentemente surgidos de forames mandibulares separados, reunindo-se em um canal único na região de molares.

Os pesquisadores observaram que as variações do tipo I foram as mais comuns, com prevalência de 0,7% da amostra total (78,8% das variações visualizadas). Os outros tipos de variações dos canais mandibulares apresentaram prevalência significativamente menor. Não foi detectada diferença na distribuição das variações em relação aos gêneros dos pacientes. Não foi possível determinar se os canais bífidos continham nervos ou somente vasos sanguíneos.

Posteriormente, Nortjé et al. (1977)[2] em revisão da amostra utilizada no estudo anterior, complementaram sua classificação, descrevendo um tipo adicional de variação dos canais mandibulares (Tabela 1). Ela consistiu de uma variação rara de canais suplementares, que não se enquadra nos tipos descritos anteriormente. Nomeada como tipo 4, esta variação consiste de uma ramificação superior, mais estreita que o ramo inferior, que não emerge na região do forame mandibular ou de nenhuma foramina própria, mas sim a partir do próprio canal mandibular, na região retromolar.

Com o intuito de estudar os canais mandibulares bífidos, Langlais et al. (1985) avaliaram amostra de 6000 radiografias panorâmicas. A prevalência encontrada foi de 0,95% (57 exames), uni ou bilaterais. Quatro tipos de canais mandibulares bífidos originados nos ramos mandibulares foram então classificados (Tabela 1), considerando suas configurações anatômicas e as suas localizações. A classificação proposta foi:

- Tipo 1: Canais bífidos unilaterais ou bilaterais, originados de um único forame mandibular, que se estendem à região de terceiros molares;
- Tipo 2: Canais bífidos uni ou bilaterais que tornam a se unir nos ramos ou corpos mandibulares.
- Tipo 3: Combinação dos tipos I e II, com cada um dos lados apresentando um tipo de canal bífido.
- Tipo 4: Canais duplos originados à partir de forames mandibulares separados.

Dentre as variações encontradas, a do tipo II foi considerada a mais comum (54,4% dos canais bífidos). Os autores relataram, ainda, que canais bífidos podem apresentar pequenos canais acessórios adicionais. Diante da variabilidade observada, os autores ressaltaram que poderiam haver outros tipos de ramificações ainda não detectadas.

Tabela 1 – Classificações das variações dos canais mandibulares, segundo Carter e Keen, 1971; Nortjé et al. 1977[1,2] e Langlais et al., 1985.

AUTORES / CLASSIFICAÇÃO	**ORIGEM**	**CARACTERÍSTICA**	**LOCAL**
Carter e Keen (1971)			
Tipo 1	Forame único	Canal único	
Tipo 2	Forame único	Canal inferior	
Tipo 3	Forame único	Canal duplicado	Ramo mandibular
Nortjé *et al.* (1977[1,2])			
Tipo 1	Forame único	Canal duplicados (medidas iguais)	Ramo mandibular
Tipo 1-a	Forame único	Canal duplicado (inferior menor)	Ramo mandibular
Tipo 1-b	Forame único	Canal duplicado (superior menor)	Ramo mandibular
Tipo 2	Forame único	Canal duplicado (superior próximo aos molares)	Ramo mandibular
Tipo 3	Foramina separada	Canal duplicado (unidos na região de molares)	Ramo mandibular
Tipo 4	Canal mandibular	Canal duplicado (unidos na região retromolar)	Ramo mandibular
Langlais *et al.* (1985)			
Tipo I	Forame único	Canal duplicado (estendendo a terceiros molares)	Ramo mandibular
Tipo II	Forame único	Canal duplicado (recorre ao canal principal)	Ramo mandibular
Tipo III	Forame único	Canal duplicado (tipo 1 e 2)	Ramo mandibular
Tipo IV	Foramina separada	Canal duplicado	Ramo mandibular

Rouas et al. (2007), comprovaram a tese de Langlais et al. (1985) de que possa haver variações dos canais mandibulares ainda não descritas. Em sua publicação, os autores relataram 3 diferentes casos de canais duplos, encontrados em uma amostra de cerca de 6000 tomografias computadorizadas realizadas para planejamento implantológico, que não encontraram classificação adequada na literatura. Sobre a origem das variações, os autores especulam que embora a teoria embrionária de Chávez-Lomelí et al. (1996) possa explicar a origem de muitas variações, não se pode desprezar a possibilidade de estarem associadas com outros fatores, como alguma alteração patológica.

Um novo tipo de ramificação do canal mandibular, não prevista nas classificações existentes, foi detectado em radiografia panorâmica e relatado por Wyatt (1996). Tratava-se de um canal mandibular suplementar, superior e paralelo ao canal principal, dirigindo-se à região distal da junção amelocementária de um terceiro molar. Embora o autor considere que classificações das variações dos canais possam não ter utilidade clínica e que possam até confundir os cirurgiões-dentistas, ele ressalta ser importante divulgar as variações anatômicas detectadas dos canais mandibulares, para que seu conhecimento possa ajudar a prevenir possíveis danos ao feixe vásculo-nervoso alveolar inferior.

Após avaliar tomografias de 122 pacientes para a detecção de ramificações dos canais mandibulares, Naitoh et al. (2009) detectaram prevalência de 65%. Baseada na análise tridimensional possibilitada pelos cortes multiplanares, as ramificações detectadas tinham origem nos ramos e foram classificadas como

- Tipo 1 (Retromolar): Ramificação ligada a forame situado na superfície óssea da região retromolar;
- Tipo 2 (Dental): Ramificação que toca os ápices radiculares dos segundos e terceiros molares;
- Tipo 3: (Para anterior): Ramificações que emergem da parede superior do canal mandibular, com ou sem confluência com o canal mandibular principal;
- Tipo 4 (Buco-lingual): Ramificação surgida da parede bucal ou lingual do canal mandibular.

As ramificações do tipo 3 (para anterior) foram as mais encontradas (44,3% dos pacientes), sendo os canais sem confluência a variedade mais comum. A segunda maior prevalência foi de canais retromolares (tipo 1), estando presente em 25,4% dos pacientes. Os canais dentais (7,4%) e os canais buco-linguais (1,6%) vieram a seguir.

2.4 - Métodos radiográficos para detecção das ramificações dos canais mandibulares

Sanchis et al (2003) detectaram uma prevalência de 0,35% de canais mandibulares em uma amostra de 2013 radiografias panorâmicas tomadas de modo padronizado. Todos os casos foram encontrados em exames de mulheres. Em posterior análise de 3 casos com ramificações em tomografias computadorizadas, foram confirmadas a ocorrência de 2 ramificações. Tal diferença evidencia a limitação dos exames bidimensionais para este propósito e lança dúvidas sobre a real prevalência das ramificações, detectadas em estudos realizados em radiografias.

Em revisão de literatura sobre a ocorrência de canais mandibulares bífidos, Claeys & Wackens (2005) reconhecem que embora as radiografias panorâmicas possam oferecer boas condições de diagnóstico, a detecção de tais variações não é frequente neste tipo de exame. Diante das importantes implicações clínicas, como dificuldades com anestesias e risco de ocorrência de neuromas traumáticos, parestesia ou hemorragias, os autores ressaltam que os cortes seccionais transversais dos corpos mandibulares, possibilitados por tomografias computadorizadas, são o melhor recurso para a identificação e localização dos canais mandibulares e de suas variações.

O relato de ramificações dos canais mandibulares não descritas na literatura, por Rouas et al. (2007), se deveu à análise tridimensional por tomografia computadorizada. Segundo os autores, as variações classificadas na literatura são baseadas em análises de radiografias panorâmicas ou outros exames radiográficos convencionais, o que pode levar a erros de diagnóstico, devido ao fato de serem exames bidimensionais, com inerente dificuldade para mostrar uma realidade tridimensional.

Dentre os casos relatados por Neves et al. (2009), foi apresentada uma radiografia panorâmica mostrando uma ramificação do canal mandibular atípica, originada no corpo mandibular e direcionada à região periapical de um molar com lesão periapical. Devido ao exame bidimensional não ter tornado possível verificar a real localização da ramificação em relação ao dente e à lesão, com vistas ao planejamento da intervenção necessária, os autores concordam que avanços nas modalidades de diagnóstico por imagem possibilitam observar e localizar os reparos anatômicos e suas variações com maior precisão e detalhamento.

Em revisão de literatura sobre a anatomia do canal mandibular e do feixe vasculonervoso alveolar inferior em relação à implantodontia, Juodzbalys et al. (2010) , detectaram que a prevalência de variações anatômicas dos canais mandibulares varia em relação ao método diagnóstico utilizado, sendo que a tomografia computadorizada tem melhor desempenho para detecção dos canais e suas variações.

Com relação à escolha do método de imagem para a identificação das estruturas vitais em Mandíbula, Juodzbalys et al. (2011) ressaltam que os critérios devem considerar a dose de radiação envolvida, o custo do exame e a confiabilidade de cada método. A TCFC, segundo os pesquisadores, mostra grande potencial, apresentando baixa dose de radiação, alta acurácia e a possibilidade de se formar imagens tridimensionais.

Kuribayashi et al. (2010), encontraram prevalências de ramificações dos canais mandibulares variando entre 0,08% e 8,3%, após revisão de estudos que avaliaram radiografias panorâmicas. Os autores realizaram, então, avaliação dos canais mandibulares em 252 TCFCs. A avaliação foi realizada por dois radiologistas, independentemente, para a detecção de canais mandibulares bífidos. Foram encontrados 47 canais bífidos, o que representou prevalência de 15,6%. A maior prevalência encontrada, comparativamente à dos estudos realizados em radiografias panorâmicas, foi creditada ao fato de a TCFC ser um exame com maior acurácia diagnóstica, devido a sua alta resolução e possibilidade de visualização tridimensional.

Comparando os protocolos de aquisição de imagens de tomografias computadorizadas multislice (TCMS) e da TCFC para o diagnóstico de lesões ósseas simuladas, Gaia et al. (2011) detectaram alta sensibilidade e especificidade de ambos métodos, sem diferenças significativas. Os autores ressaltaram a importância da reconstrução multiplanar e de cortes transversais possibilitados pelas tomografias para esta finalidade.

Considerando a identificação do canal mandibular como importante pré-requisito para a realização de procedimentos na região posterior da mandíbula, Oliveira-Santos et al. (2011) avaliaram a acurácia de cortes transversais de tomografia computadorizada para este propósito. Os resultados mostraram que o CM foi visível em 53% das hemi-mandibulas analisadas. Dificuldade ou muita dificuldade para a sua detecção foram registradas em até 25% das amostras. Não foram detectadas diferenças de visualização entre áreas com ou sem dentes. A discriminação do CM em relação às estruturas adjacentes ficou menos óbvia nos cortes situados nas proximidades do forame mentual.

Rodella et al. (2012) revisaram estudos dos canais mandibulares publicados até 2011, na base de dados PubMed, incluindo estudos radiográficos, anatômicos e clínicos. As prevalências de variações dos canais mandibulares foram variadas (0,1% a 65%), assim como as classificações. Os autores acreditam que as diferenças de prevalência podem se dar em decorrência das metodologias utilizadas, já que alguns estudos analisaram exames radiográficos bidimensionais enquanto outros realizaram estudos em tomografias computadorizadas.

Oliveira-Santos et al. (2012) examinaram 100 tomografias realizadas em um tomógrafo de feixe cônico, coletadas de modo randomizado. As hemi-mandíbulas foram avaliadas em cortes multiplanares para analisar os canais mandibulares. Registros de falsos canais mandibulares, como a impressão do nervo milohióideo na superfície lingual da mandíbula, foram cuidadosamente evitados. Canais mandibulares bífidos, com diâmetro maior que 1 milímetro (mm) foram observados em 19% das amostras. Não foram encontradas diferenças estatisticamente significativas entre gêneros, idade ou lados. Considerando que os resultados de pesquisas anteriores baseadas em exames convencionais apresentaram menor prevalência, os autores acreditam que estes exames não são confiáveis para a detecção de variações dos canais mandibulares. Devido aos falsos diagnósticos em exames convencionais, os autores alertam para a importância de se realizar as avaliações combinando diferentes reconstruções, para se assegurar sobre sua anatomia. Analisando os cortes transversais, os autores relatam que a visibilidade dos canais mandibulares é maior nas regiões posteriores, principalmente na região dos primeiros molares (66%), decrescendo gradualmente até as proximidades do forame mentual.

Em análise comparativa da acurácia diagnóstica entre tomografias computadorizadas de feixe cônico e radiografias panorâmicas, Muinelo-Lorenzo et al, (2014) observaram que as radiografias panorâmicas foram capazes de identificar somente 37,8% das ramificações dos canais mandibulares identificadas nas tomografias.

2.5 - Conteúdo das ramificações dos canais mandibulares

Como a avaliação dos canais mandibulares e de suas variações anatômicas por meio de exames de imagem não permitir saber qual é o conteúdo das ramificações, Ikeda et al. (1996) avaliou canais mandibulares de hemimandíbulas de cadáveres congelados por meio de ressonância magnética e posterior avaliação histológica. Embora reconheçam que a utilização de peças anatômicas congeladas altere as condições de avaliação, comparativamente à realidade clínica, os autores conseguiram diferenciar o tecido neurovascular situado no interior dos canais e o tecido conjuntivo circundante e concluíram que a ressonância magnética é um eficiente método para a localização dos canais mandibulares e determinação de seu conteúdo.

Em relato de caso de uma rara variação anatômica do forame mentual, originada de uma bifurcação do canal mandibular principal, emergindo na face lingual, Neves et al. (2010) supõem a presença do feixe vásculo nervoso alveolar inferior, devido a sua origem. Segundo os autores, algumas foraminas que não têm origem em bifurcações do CM são, na realidade, foraminas nutritivas, com presença apenas de vasos sanguíneos.

O nervo alveolar inferior pode originar múltiplos ramos extraósseos antes de adentrar a mandíbula e a ocorrência de foraminas acessórias e de múltiplos canais podem estar associadas com essas variações. O nervo alveolar inferior pode também estabelecer comunicação com os outros ramos da divisão mandibular, como o nervo milohióideo (Bennett & Towsend, 2001). Ainda assim, não há certeza se as variações dos canais mandibulares contêm ramos neurovasculares ou apenas vasos sanguíneos (Rodella et al., 2012).

Esclarecendo especulações sobre o conteúdo das ramificações dos canais mandibulares, tendo em vista a possibilidade de representarem canais nutritivos e conterem apenas vasos sanguíneos, Fukami et al (2012) realizaram avaliação histológica de ramificações retromolares e confirmaram a presença de estruturas neurovascular em seu interior. Tal achado reforça a tese de que variações dos canais mandibulares representam considerável risco em procedimentos cirúrgicos e que possam estar relacionadas com alterações na sensibilidade mandibular e com a susceptibilidade à anestesia.

2.6 – Neurogênese, angiogênese e inflamação

A neurogênese e a neuroplasticidade são fenômenos que despertam grande interesse científico, devido às necessidades de desenvolvimento de terapias para a reparação nervosa.

Contrariando a concepção de que as radiolucências periapicais não são inervadas, Lin & Langeland (1981), em avaliação por microscopia eletrônica detectaram feixes nervosos mielinizados e não-mielinizados em locais com inflamação aguda ou crônica. Não foi possível determinar a razão de as fibras nevosas serem resistentes ao processo inflamatório. Os achados podem ajudar a explicar as dificuldades com procedimentos anestésicos de dentes com polpa comprometida por inflamação.

Lindholm et al. (1987) verificaram que após a lesão de nervos ciáticos de cobaias houve aumento acentuado nas quantidades de fatores de crescimento neuronais liberados, comparativamente às regiões sem lesão. A quantidade de fatores de crescimento neuronal detectada nos nervos após as lesões foi comparável àquela presente nos nervos ciáticos de cobaias recém-nascidas. Os macrófagos apresentaram importante papel na regulação da síntese desses fatores. A ação de macrófagos ativados pôde ser mimetizada por condicionamento do meio por interleucina-1, um mediador envolvido em processos inflamatórios.

A resposta de fibras nervosas à inflamação foi avaliada induzindo pulpites e lesões periapicais artificialmente. A análise imunohistoquímica mostrou aumento da quantidade das fibras nervosas e alterações dos axônios neuronais nos tecidos em torno dos locais com inflamação periodontal e necrose. Os resultados mostraram que há interações entre as fibras nervosas e a inflamação e sugerem algum papel das estruturas nervosas na inflamação neurogênica, nas condições para a ocorrência de inflamação crônica, na dor e nas dificuldades com anestesia em presença de inflamação (Kimberly & Byers, 1988).

O estudo imunohistoquímico de Henry et al. (1993) detectou a presença de receptores de fatores de crescimento nervosos em tecidos neuronais do ramo mandibular do trigêmeo, após lesão artificialmente provocada na raiz dorsal do nervo, e contribuiu para prover mais uma evidência sobre possível capacidade de regeneração neurovascular na região orofacial.

A possibilidade de neurotransmissores agirem na indução da neurogênese foi demonstrada por Albers et al (1994) em avaliação histoquímica e imunohistoquímica. O estudo experimental baseou-se na avaliação da ação de um fator de crescimento neuronal e demonstrou ser possível a ocorrência de neurogênese no sistema nervoso periférico na pele de cobaias transgênicas.

Há exemplos dessa interação envolvendo os tecidos de interesse odontológico, como a influência de estruturas neuronais sobre a odontogênese (Christensen et al., 1993), a reorganização e proliferação nervosa na região periapical de dentes pulpectomizados (Holland, 1985) e a regeneração neuronal de terminações de Ruffini, localizada no ligamento periodontal após injúria artificialmente criada no nervo alveolar inferior de ratos (Youn et al. (1997).

Avaliação imunohistoquímica demonstrou que houve aumento na densidade de nervos pulpares e de células dendríticas envolvidas na reação imune em dentes acometidos por cárie superficial. Após a formação de dentina reparativa, essa densidade foi menos pronunciada. Esse fenômeno sugere que uma interação neuro-imune parece desempenhar significante papel na modulação de processos patológicos em polpas dentárias. (Sakurai et al., 1999).

Axônios invadem o gânglio trigeminal e envolvem neurônios sensoriais de cobaias com aumento da expressão de fatores de crescimento neuronal. Este crescimento axonal parece ser direcional e específico. Walsh et al (1999), em estudo sobre a ação de um neuromediador específico (p75) neste fenômeno, indicam que ele não é necessário para iniciar ou sustentar o crescimento axonal, mas desempenha um papel na regulação do direcionamento deste crescimento.

Baseado nos princípios de biologia molecular, avançados métodos de diagnóstico por imagem têm sido desenvolvidos para permitir a avaliação das estruturas neurais. Tais exames têm possibilitado demonstrar e avaliar a ocorrência de neurogênese e neuroplasticidade em regiões afetadas por inflamação, criando novos paradigmas para o estudo de neurobiologia (Thiyagarajan et al., 2008).

A influência de um fator de crescimento neuronal que desempenha papel como mediador em processos inflamatórios foi avaliada para o aumento da densidade de fibras sensitivas nervosas. O estudo experimental em cobaias transgênicas comprovou a relação da proliferação nervosa com a expressão desse mediador Schnegelsberg et al. (2010).

Superando estudos *post-mortem* que alegavam impossibilidade de reparação de lesões nervosas por falta de potencial reparador de neurônios e de possível ação de inibidores de crescimento, a avaliação de imagens de cobaias *in vivo*, por Di Maio et al. (2011), possibilitaram a avaliação dos fenômenos envolvidos em lesões neurais e criaram novo paradigma para a evolução destes casos. As técnicas utilizadas pelos autores, com uso de marcadores fluorescentes, mostraram que as falhas na reparação de lesões nervosas estão mais associadas com a formação de barreiras físicas no local da lesão do que propriamente pela incapacidade de regeneração de neurônios. Tal descoberta leva ao melhor entendimento do mecanismo fisiológico de reparação nervosa, e contribui para o desenvolvimento de terapias que possam induzir ou auxiliar a reparação destas lesões.

Evidências desse fenômeno em tecidos humanos foram detectadas por Lee et al. (2011) quando avaliaram a ação de citocinas inflamatórias catabólicas na expressão de genes envolvidos na produção de fatores relacionados à angiogênese e neurogênese. Análise imunohistoquímica dos tecidos de pacientes com degeneração de discos intervertebrais mostrou correlação positiva entre as citocinas e a expressão dos genes. A avaliação da expressão do RNA das amostras sugere que as citocinas são geradas pelo processo inflamatório e estimulam a invervação e neovascularização dos discos.

Com o objetivo de discutir a resposta do hospedeiro em casos de periodontites apicais, com foco na produção de citocinas, Graunaite et al. (2011) revisaram artigos publicados na língua inglesa de 1999 a 2010, além de livros e jornais. Considerando os mecanismos envolvidos na etiopatogenia das lesões, assim como na resposta imune inata, concluíram que a abundância de interações de várias moléculas anti-inflamatórias pode influenciar a produção de citocinas, alterar a progressão das patologias, assim como a degradação dos tecidos perirradiculares.

Oshima et al. (2011) detectaram que a presença da enterotoxina B, derivada de bactérias do gênero Staphylococcus, aumenta a inervação por fibras sensoriais do tipo C em peles de ratos. Provavelmente por aumentar a produção de neurotrofinas, incluindo o fator de crescimento nervoso, uma vez que esta toxina ocasiona inflamação neuronal. Os autores suspeitam que a ativação de células T induzida pela enterotoxina pode iniciar esse fenômeno.

Ao analisar granulomas e cistos periapicais por meio de reações imunoistoquímicas, Fonseca-Silva et al. (2012) detectaram a presença do fator de crescimento endotelial relacionado ao desenvolvimento dessas lesões. De maneira consistente com os mecanismos imunes relacionados com as lesões, concluiu-se que a angiogênese desempenha papel fundamental na etiopatogenia das alterações inflamatórias crônicas. Além da detecção do fator de crescimento endotelial, a densidade da microcirculação sanguínea e o número de células de defesa também foram pesquisados. A predileção da localização de ambos foi em torno de vasos e nervos locais, indicando que a angiogênese e a quimiotaxia se dão a partir de feixes vásculo-nervosos locais.

A fim de melhor avaliar a terapia com células-tronco para o tratamento de derrames, Scheller et al. (2014) testaram exames de imagem não invasivos por ressonância magnética ultra-sensível e microscopia a laser. Tais exames se mostraram eficientes e possibilitaram avaliar a sequência de eventos e as complexas interações celulares promovidas pelo tratamento. Com isso, se tornou possível analisar a ação da neuroinflamação, o principal obstáculo para a ocorrência de neurogênese endógena e a neurogênese exógena promovida pela terapia com células precursoras.

3 - Objetivos

3.1 Objetivo Geral

Avaliar a ocorrência de ramificações dos canais mandibulares e de lesões inflamatórias, diagnosticadas por tomografia computadorizada por feixe cônico.

3.2 Objetivos específicos

- Determinar a prevalência de ramificações dos canais mandibulares.
- Avaliar e descrever as características morfológicas das ramificações dos canais mandibulares detectadas, assim como sua localização e a presença de foraminas adicionais.
- Determinar a prevalência de lesões inflamatórias nas regiões com ramificações dos canais mandibulares.
- Avaliar e descrever os tipos e a localização de lesões inflamatórias detectadas.
- Avaliar os níveis de cinza nas regiões com ramificações dos canais mandibulares.
- Avaliar a relação estatística das ramificações dos canais mandibulares com os gêneros dos pacientes, com as lesões inflamatórias detectadas e com os níveis de cinza nas regiões de acometimento.

4 - Hipóteses

Sugere-se um aumento na prevalência de ramificações dos canais mandibulares nas regiões dos corpos mandibulares, quando da presença prévia de lesões dentárias inflamatórias, comparativamente aos indivíduos sem lesões.

Sugere-se que os níveis de cinza das regiões com ramificações dos canais mandibulares não exerçam influência na acurácia diagnóstica das ramificações dos canais mandibulares.

5 - Metodologia

Para o presente estudo, foram obtidas aprovações do Comitês de Ética em Pesquisa da Universidade Federal de Minas Gerais (Brazil - COEP 432.2982) e da Universidade de Alberta (Canada - Pro00050422).

5.1 - População de estudo

TCFC de mandíbulas foram obtidas da base de dados do Serviço de Imaginologia Odontológica de um centro de diagnóstico por imagem (Departamento de Imagem e Diagnóstico Molecular Hermes Pardini - Belo Horizonte, Brasil) e da base de dados do Departamento de Odontologia da Universidade de Alberta (Edmonton, Canadá).

As imagens foram realizadas com finalidade diagnóstica, sendo formalmente requisitadas pelos cirurgiões-dentistas responsáveis pelos pacientes. O presente estudo avaliou o total de 2.484 TCFCs, sendo 1.307 do Brasil e 1.177 canadenses.

Todos os exames foram realizados em tomógrafo I-CAT® (Next Generation Model – Imaging Sciences International – Hatfield, PA, EUA). As imagens do Brasil foram adquiridas usando tamanho de voxel igual a 0,25 milímetros (mm), campo de visão (*FOV*) igual a 7x16 centímetros (cm) e tempo de exposição de 26,9 segundos. As imagens canadenses tiveram tamanho de voxel igual a 0,3 mm, *FOV* igual a 13x16 cm e tempo de exposição de 8,9 segundos. As diferenças de tamanho de voxel, *FOV* e tempo de exposição foram devidas às diferentes indicações clínicas para o exame.

Os exames de ambas as bases de dados foram analisados para detectar a presença de RCM emergindo do canal mandibular. As análises foram realizadas em reconstruções panorâmicas (com espessuras entre 5,25 mm a 10,25 mm) e cortes multiplanares (com espessuras de 1 mm e espaçamentos de 1 mm), usando o programa Xoran® (Xoran Technologies - Ann Arbor, MI, EUA).

As avaliações foram realizadas pelo pesquisador, especialista em Radiologia e Imaginologia Odontológicas há 12 anos, sendo executadas em monitor *LED* de 20 polegadas, com resolução de 1600x900 pixels (Flatron E2442TC model - LG Electronics – Seul, Coréia do Sul).

5.2 Variáveis analisadas

As 2.484 TCFCs foram avaliadas para a presença, número e localização de RCM, considerada como variável dependente. As seguintes variáveis independentes foram registradas em banco de dados: gênero, idade, presença de lesões inflamatórias, localização das lesões inflamatórias e o nível de cinza na região com RMF e ou lesão inflamatória.

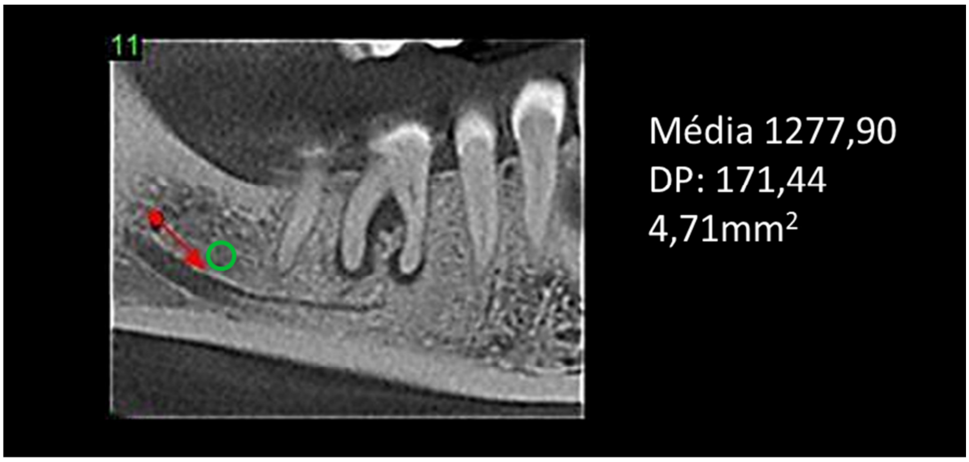
A localização de lesões inflamatórias e de RCM foi observada no ramo mandibular, região retromolar, região de molares ou região de pré-molares, de acordo com o local de ocorrência das lesões ou do sítio de emergência da RCM do canal mandibular principal.

O diagnóstico de lesão inflamatória foi realizado em conjunto com a avaliação dos formulários de requisição de exames dos pacientes. Estas foram confirmadas nas TCFCs e foram consideradas como: 1) lesões periapicais, localizadas junto aos ápices radiculares, com origem endodôntica; 2) osteólises circundando raízes, representando lesões endoperio; 3) perdas ósseas verticais e ou horizontais, as quais representaram doenças periodontais típicas; 4) osteólises circundando implantes, representando ausência de osseointegração; 5) sítios de reabsorções radiculares externas inflamatórias, concomitantes com imagens hipodensas adjacentes; 6) espessamentos dos espaços correspondentes aos ligamentos periodontais, como sinais adicionais de pericementite; e/ou 7) espessamento dos espaços correspondentes aos folículos pericoronários de dentes inclusos e impactados, como aspecto adicional de pericoronarite. Em casos de doença periodontal com perda de inserção óssea horizontal generalizada, toda a região posterior da mandíbula foi considerada como a localização da lesão.

A localização das RCM foi definida como o sítio em que as ramificações emergiram do canal mandibular. O número total de ramificações em cada paciente e a ocorrência de contato entre uma dada lesão inflamatória e uma RCM foram também registradas. De acordo com suas características, as RCM foram classificadas como: 1) número: simples, duplas ou múltiplas, considerando o número de ramificações surgindo de um único canal mandibular; 2) orientação: superior, inferior, vestibular ou lingual, de acordo com a direção que seguiram após emergirem do canal mandibular; 3) conexão com lesões inflamatórias: quando as terminações das RCM estabeleceram ou não contato com as lesões; 4) local de conexão com as lesões: terços cervical, médio ou apical das raízes que apresentaram lesões.

A ferramenta de níveis de cinza provida pelo programa de manipulação de imagens foi aplicada em cortes sagitas com 01 mm de espessura, posicionados alinhados com o trajeto do canal mandibular. As mensurações da região de interesse (*ROI*) foram padronizadas com área igual a 4,71 milímetros quadrados (mm^2). Nos exames com RCM as mensurações foram situadas no osso medular situado exatamente acima da origem das ramificações (Figura 1). Nos exames sem a presença de RCM as medidas foram executadas em um dos corpos mandibulares, selecionado aleatoriamente, exatamente acima do canal mandibular, em ponto situado apicalmente em relação à raiz mesial do primeiro molar, considerado como o centro da região posterior do processo alveolar.

Figura 1 - Mensuração do nível de cinza (grupo casos)incluir área de análise trocar média apor valor 10x15



5.3 Avaliação da concordância intra-examinador e cálculo amostral

Avaliação da concordância intra-examinador e cálculo amostral foram realizados avaliando 15 TCFCs, aleatoriamente selecionadas (5 exames com RCM e 10 exames sem RCM), repetindo as avaliações por três vezes, com intervalos de 15 dias entre as avaliações. O teste Kappa foi aplicado para verificar a confiabilidade intra-examinador e detectou concordância classificada como “Quase Perfeita” para o diagnóstico de RCM (I=0,842) (Landis & Koch, 1977). As imagens utilizadas para esta avaliação prévia não foram incluídas na amostra final do estudo principal.

Para o estudo de casos e controles, a amostra com 50 casos e 100 controles garantiu um poder de teste de 99.9% e nível de confiança = 95% (Harvey & Lang, 2010). As TCFCs foram então divididas nos grupos:

1) Grupos casos: 50 exames apresentando RCM emergindo do canal mandibular na região abaixo dos dentes posteriores (região de molares ou pré-molares);
2) Grupo controles: 100 TCFCs sem sinais de RCM. Como os canais sem ramificações apresentam maior prevalência, foi adotada uma proporção de dois controles para cada caso.

Gênero e idade foram pareados. O grupo casos teve 23 homens e 27 mulheres (média de idade = 50,88 anos). O grupo controles teve 41 homens e 59 mulheres (média de idade = 50,33 anos).

Apenas um dos lados das mandíbulas dos pacientes foi incluído na amostra final, para se evitar alteração no número de pacientes de cada grupo. No grupo casos, se houve RCM em ambos os lados, apenas um deles foi aleatoriamente selecionado.

5.4 Análise estatística

O teste-T para amostras independentes foi usado para comparar a acurácia diagnóstica para a identificação de RCM em ambas as bases de dados. Houve homogeneidade de variância entre elas, estatisticamente significante (P=0,122), indicando que as diferenças dos tamanhos de voxel, *FOV* e tempo de exposição das bases de dados não tiveram influência na acurácia diagnóstica para a identificação de RCM.

A idade da amostra foi dicotomizada pela mediana à fim de verificar se houve diferença na ocorrência de RCM em pacientes mais jovens ou mais velhos.

A análise estatística foi realizada usando o programa *Statistical Package for Social Sciences* (SPSS – 22.0, IBM, Armonk, NY, EUA), com nível de significância ajustado para 5% ($p<0.05$). O teste de Kolmogorov foi usado para verificar a distribuição da amostra. O teste T, teste do Qui-quadrado ou teste exato de Fisher foram usados para avaliar as diferenças estatísticas entre a ocorrência de RCM e as variáveis independentes.

Para o estudo de casos e controles foi aplicada a análise bivariada, considerando 95% de intervalo de confiança (95%). As variáveis com valor de $p \leq 0,2$ foram incorporadas em análise de regressão logística e aquelas que subsequentemente apresentaram valor de $p<0,05$ foram consideradas significantes e permaneceram no modelo final (Hosmer & Lemeshow, 2004).

6 – Resultados e Discussão

6.1 Artigo 1 – Publicado na revista "World Journal of Radiology"

TITLE: Classifications of mandibular canal branching: a review of literature

RUNNING TITLE: Classifications of mandibular canal branching

KEYWORDS: Inferior alveolar nerve; mandibular canal; bifid mandibular canal; dental radiography; cone-beam computed tomography.

Abstract

AIM: To gather existing radiographic classifications of mandibular canals branching, considering the criteria on which these were based.

METHODS: The search for studies on mandibular canals based on imaging exams included literature reviews, epidemiological studies of prevalence, descriptive studies, or case reports. An electronic search in the Medline (OvidSP), Pubmed, Embase (OvidSP), Web of Science (Thompson Reuters), and Scopus (Elsevier) databases was performed, as well as a manual evaluation of the references of the selected articles. Combinations of key words were placed in each database. No restrictions were imposed regarding the year of publication or language. References collected in duplicate were removed by the authors. A table was drawn up, containing the included studies and respective interest data.

RESULTS: Six classifications of mandibular canals branching were selected for the present literature review. Four were based on two-dimensional radiographic exams, and two were performed based on three-dimensional tomographic exams. Three-dimensional classifications were determined based on the analysis found in the least number of exams, comparatively to two-dimensional studies. The prevalence of mandibular canal branching varied from 0% to 38.75% in the works based on two-dimensional exams, while those found in three-dimensional exams ranged from 15.6% to 65%. The studies were mostly referred to branches that began in the mandibular ramus. Just one classification considered the branches that began in the mandibular body region.

CONCLUSION: Three-dimensional exams appear to be the best method to view mandibular canal branching. Further studies are warranted to determine its true prevalence and questions concerning to associations.

Key Words: Inferior alveolar nerve; mandibular canal; bifid mandibular canal; dental radiography; cone-beam computed tomography.

Core Tip: The identification of the mandibular canal and its branching are important for the planning of dental procedures. Due to the limitations of the two-dimensional exams, the three-dimensional view of the structures provided by computed tomography (CT) exams allowed for greater sensitivity for the detection and evaluation of mandibular canals. Nevertheless, some studies performed with CT exams continued to use the classifications based on two-dimensional exams. Given the variability of information on this aspect, this study aimed to gather existing information in an attempt to provide researchers and clinical professionals with a stronger basis for their studies and procedures.

INTRODUCTION

Mandibular canals are intraosseous ducts, normally unique in each hemimandible. These begin in the mandibular foramen, located in the lingual surfaces of the mandibular bodies and stretch until they emerge in the mental foramen, in a vestibular direction in the pre-molar region. Located inside of these canals is the inferior alveolar neurovascular bundle, the largest ramus of the mandibular division of the trigeminal nerve, responsible for the innervation of the posterior teeth, of the surrounding bone structure, and of the mucosa of the tongue coating of the posterior region[1].

The identification of the mandibular canal is important for the planning of a wide range of dental procedures, especially surgical procedures. The insertion of implants, extraction of impacted teeth, surgical planning of biopsies, enucleations of pathologies, orthognathic surgeries, and the defining of differential diagnoses are only a few examples of the clinical importance of its localization[2-7]. The occurrence of anatomical branching in mandibular canals constitutes a complicating factor and requires care for the proper planning of such cases in order to avoid inferior alveolar neurovascular bundle lesions.

As this study treats intraosseous anatomic structures, imaging exams are recognized as the main diagnostic resource for their localization and evaluation. The radiographic study of human fetal mandibles, performed by Chávez-Lomelí et al.[8], detected that bifid or trifid canals are the main anatomical branching of the mandibular canals. For this reason, radiographic classifications were developed according to conventional exams. These systems considered their origins, localization, aspect, and direction as core criteria[1,9-12]. Due to the limitation inherent to the two-dimensional exams, Langlais et al.[11] contemplated the possibility of the existence of undetected or undescribed canals.

The three-dimensional view of the structures provided by computed tomography (CT) exams allowed for greater sensitivity for the detection and evaluation of mandibular canals, in addition to the three-dimensional classification of the mandibular canal. CT studies have presented different prevalence levels and other types of mandibular canal branches[13-15]. Nevertheless, some studies performed with CT exams continued to use the classification of the variation of mandibular canals based on two-dimensional exams[14,16].

Bearing this finding in mind, the present review seeks to list the classifications and descriptions of the branching of existing mandibular canals, considering the applied diagnostic resources and the criteria on which these were based. Given the variability of information on this aspect, as well as the prevalence and classification, this study aimed to gather existing information in an attempt to provide researchers and clinical professionals with a stronger basis for their studies and procedures.

MATERIALS AND METHODS

Eligibility criteria

This literature review proposed the search for radiographic studies on mandibular canals in humans, based on conventional and digital two-dimensional exams and on CT exams. This work included literature reviews, epidemiological studies of prevalence, descriptive studies, or case reports. No letters to the editor, animal studies, abstracts, or personal opinions were included.

Sources

This study performed an electronic search in the Pubmed, Embase, Web of Science (Thompson Reuters), and Scopus (Elsevier) databases. The references of the selected articles were also manually evaluated to detect relevant studies that might have been lost in the electronic search. A complementary search was also conducted using Google Search and Google Scholar search tools.

Research Strategy

Combinations of key words were placed in each database, using the following key words: mandible, mandibular nerve, inferior alveolar nerve, mandibular canal, bifid mandibular canal, bifid canals, radiography, panoramic radiography, cone-beam computed tomography, dental implant, and anatomic variation. No restrictions were imposed regarding the year of publication or language. References collected in duplicate were removed by the authors.

Study selection

After having removed the duplicates, the abstracts of all of the chosen articles were read to verify the appropriateness of the theme. The main objective was to find articles that defined the classification of mandibular canal branching. After having selected the articles that met the eligibility criteria, these were read in full and incorporated into the present review.

Synthesis of the collected data

A table of the included studies was drawn up, containing the following data: authors' names, year of publication, sample size, exam per image used in each study, prevalence of mandibular canal branching, and description of the defined classification, including the name adopted for the branches, the frequency of each type, the location of origin, aspect, direction, and end location.

RESULTS

Six radiographic classifications of the branching in mandibular canals were selected for the present literature review (Table 1)[1,9-12,14-15].

Within the listed classification, four were defined by evaluating the canals and their branching in two-dimensional radiographic exams[1,9-12], and two were performed based on three-dimensional CT exams. Two of the classifications based on two-dimensional evaluations also conducted dissections of the anatomical parts[10,12].

The classifications based on two-dimensional exams were carried out by analyzing the samples with the highest number of exams (9,717 in total, with an average of 2,429.25 exams). Nortjé et al.[1,9] evaluated 3,612 panoramic radiographs, while Langlais et al.[11] evaluated 6,000 exams. Three-dimensional classifications were determined based on the analysis found in the least number of exams (374 in total, with an average of 187 CT exams).

The prevalence of the mandibular canal branching varied from 0% to 38.75% in the works based on two-dimensional exams, with an average of 10.15%. The prevalence of branches found in CT exams ranged from 15.6% to 65%, with an average of 40.3%.

Only the classification defined by Kieser et al.[12] considered the branches that began in the mandibular body. All others referred to those initiated in the mandibular ramus.

DISCUSSION

Radiographic studies of the prevalence branching in mandibular canals presents variability, ranging from 0.08%[17] to 38.75%[10] when based on two-dimensional exams, and from 15.6%[14] to 65%[15]. This variability is related to the use of different methods, including panoramic radiographic evaluations and CT exams.

Claeys and Wackens[18] warned that, although panoramic radiographs offer diagnostic conditions, the recognition of the branching in mandibular canals is rare. The authors defined that the cross-sectional cuts of the mandibular bodies, made possible through CT exams, were the best method to identify and locate their route. In an attempt to establish a more efficient method, capable of detecting the real prevalence and localization of these alterations, the CT exam has truly sparked great progress and has proven to be better as regards the limitations presented by the panoramic radiographs[3,15,19]. For this reason, it is recommended as the method of choice for the planning of a wide range of surgical procedures in dentistry[20].

However, the comparison among the methods reaches beyond that referent to the absolute prevalence of the occurrence of anatomical branching in mandibular canals. The comparison of the prevalence of different types of canals detected in panoramic radiographs and in the three-dimensional exams is of outmost importance due to the highest and lowest clinical significance that each type can represent. Furthermore, this comparison is made more difficult by the lack of a standardization of the classifications adopted in the different studies. The classification of the branches detected through tomographic exams[15-16,21-22], though similar to those from two-dimensional exams, presented some differences and some new criteria[1,10-12].

In one three-dimensional exam, Kuribayashi et al.[14], although they had defined an additional classification criterion by evaluating the diameter of the branches of the mandibular canals in relation to the main canal, primarily used the two-dimensional classification set forth by Nortjé et al.[1] for detected canals. Their results pointed towards a greater prevalence of mandibular canal branching when compared to that found by Nortjé et al.[1] Moreover, when compared to the diverse types of branches, a difference could also be observed regarding the most prevalent type of canal. While Nortjé et al.[1] found greater prevalence for type I bifid canals (78.8%), Kuribayashi et al.[14]found a greater prevalence of type II branches (13.2%).

Likewise, Correr et al.[16] used the two-dimensional classification, as defined by Langlais et al.[11], for a tomographic evaluation of mandibular canal branching. It was not possible to compare the prevalence of these studies, given that the samples evaluated by Correr et al. [16] consisted, in its totality, of previously diagnosed exams referent to the occurrence of branches. However, as regards the proportion among the different types of branches, differences were observed. The type I standard was the most commonly detected in tomographic exams (72.6%), followed by the type II (19.3%), whereas the types I and II were detected in 38.6% and 54.4% of the panoramic radiographs, respectively. No type IV branches were detected in the scans.

These results reveal the existence of differences in the diagnostic accuracy of the methods. Nevertheless, the analysis of the different two- and three-dimensional classifications calls attention to some other relevant differences. As regards the evaluation of the diameters of the branches referent to the main canals[14], this can contribute to the greater or lesser relevance of the findings. While higher caliber branches may represent a greater risk of injury, one must also bear in mind that the branches of a lesser volume may be referent to nutrient canals, such as that found in the dissections performed by Carter and Keen[10].

Another aspect to be considered refers to the direction of the branches. Whereas the two-dimensional classification includes the description of the direction only in the anteroposterior and superoinferior directions, the three-dimensional classification set forth by Naitoh et al.[15] is also concerned with the situation of the branches in the vestibular-lingual direction. This is an important factor to be considered in the surgical planning of cases[2,6,23-24] thus contributing to improvements in the definition of the localization of the surgical access route as well as better estimations of the risk of injury to the surrounding anatomical structures.

In conclusion, the detection of mandibular canal branching is important to determine the proper conduct to be taken with patients with dental problems, and imaging exams represent the standard method to view these alterations. Three-dimensional exams appear to be the best method, however, further studies are warranted to determine the true prevalence these alterations, some possible associated factor, and other such questions concerning three-dimensional systems.

Table 1 - Classifications of mandibular canal branching (1971-2010)

Autors	**Exam**	**Sample**	**Prevalence (mandibular canal branching)**	**Classification**	**Frequency of the types**	**Region of origin**	**Aspect**	**Direction**	**Local of termination**
Carter & Keen (1971)[10]	Unilateral radiographs and dissection	80	38,75%	Type 1	61,25%	Ramus region, from a single Mandibular Foramen	Single large structure with very short dental branches	Superior to the tips of molars roots	Mental arborization.
				Type 2	13,75 % (types 1 or 2)	Ramus region, from a single Mandibular Foramen	Substantially lower down, with dental branches given off more posteriorly, longer and oblique	Oblique, toward the tips of molars roots.	Mental arborization.
				Type 3	25% (types 2 or 3)	Ramus region, from a single Mandibular Foramen	Two large branches initiated posteriorly	Uppers like alveolar branches	Upper to the tips of the roots. Lower to mental forame.
Nortjé et al. (1977)[1]	Panoramic radiographs	3612	0.9	Type 1a	30.3% of duplication cases	Ramus region, from a single Mandibular Foramen	Two canals of a similar width (lower slightly narrower)	Inferior narrower.	
				Type Ib		Ramus region, from a single Mandibular	Double (Superior narrower)	Anterior	

						Foramen			
				Type II		Ramus region, from a single Mandibular Foramen	Duplo (Superior shorter)	Anterior	Superior: toward 2nd and 3rd molars and inferior: toward mental foramen
				Type III		Ramus region, from separated Mandibular Foramens	Double (join in the molars region)	Anterior	Molars region
Nortjé et al (1977)[9]		3612		Type IV		Ramus region, from a single Mandibular Foramen	Double (Superior narrower than the main canal)	Anterior	Ramus region.
Langlais et al (1985)[11]	Radiografias panorâmicas convencionais	6000	0,95	Type I	38,6%	Ramus region, from a single Mandibular Foramen	Double (Superior shorter)	Anterior	3rd molar and adjacente region.
				Type II	54,4%	Ramus region, from a single Mandibular Foramen	Double (Joining anteriorly)	Anterior	Ramus or mandibular body regions.
				Type III	3,5%	Ramus region, from a single Mandibular Foramen	Double (Combination of types II and III)	Anterior	Ramus, retromolar ou 3rd molar regions.

				Type IV	3,5%	Ramus region, from separated Mandibular Foramens	Double (Joining anteriorly)	Inferior	Ramus region.
Kieser et al (2005)[12]	Oclusal and unilateral radiographs and dissection	107 mandibles (25 radiographic exams)	0%	Type I (detected by mean of dissections and radiographs)		Ramus region, from a single Mandibular Foramen	Single, without branches	Anterior	Mental foramen region.
				Type II (detectado em dissecações)		Mandibular body region	Series of individual branches	Superior	Alveolar process (Edentulous mandibles)
				Type III (detectado em dissecações)		Molars region	Molar plexus	Superior	Molar region (Edentulous mandibles)
				Type IV (detectado em dissecações)		Distal and proximal regions	Distal and proximal plexus	Distal plexus forward. Proximal plelxus toward superior.	Alveolar process (Edentulous mandibles).
Naitoh et al (2009)[15]	CBCT	122	65%	Type 1 Retromolar	29,8%	Ramus region	Superior	Superior	Retromolar region.
				Type 2 Dental Canal	7%	Ramus region	Superior	Anterior	Root Apex of the third molar.

				(3º molar)					
				Type 2 Dental Canal (2º molar)	1,8%	Ramus region	Superior	Anterior	Root Apex of the second molar.
				Type 3 Forward Canal (with confluence)	4,5%	Ramus region	Superior (Joining to the main canal)	Anterior	Mandibular body.
				Type 3 Forward Canal (without confluence)	55,3%	Ramus region	Superior	Anterior	Mandibular body.
				Type 4 Buccal or lingual canal	1,8	Ramus region	Lateral	Inferior (Buccal or lingual)	Ramus region.
Kuribayashi et al (2010)[14]	CBCT	301 unilateral exams from 252 patients	15,6%	Less than 50% of the diameter of the main canal	51%		Narrower (Less than 50% of the diameter of the main canal)		
				Equal or bigger than 50% of the diameter of the main canal	49%		Equal or bigger than 50% of the diameter of the main canal		

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6.2 Artigo 2 – Submetido a "World Journal of Radiology"

TITLE: Tomographic assessment of mandibular canal branching in regions with dental inflammation

RUNNING TITLE: Mandibular canal branching and dental inflammation

KEYWORDS: Inferior alveolar nerve; mandibular canal; bifid mandibular canal; dental radiography; cone-beam computed tomography.

Manuscript Type: RETROSPECTIVE STUDY

Tomographic assessment of mandibular canal branching in regions with dental inflammation

Castro MAA et al. Mandibular canal branching and dental inflammation

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Conflict-of-interest statement: All the authors declare that they have no competing interests.

Data sharing: Technical appendix, statistical code and dataset are available from the corresponding author at mauaac@yahoo.com.br Participants gave informed consent for data sharing, but the present data are anonymized and risk of identification is low.

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Abstract

AIM: To investigate mandibular canal branching (MCB) in alveolar ridges with dental inflammation by means of cone beam computed tomography (CBCT).

METHODS: A database of 2,484 CBCTs was reviewed for identifying dental inflammation in mandibular alveolar ridges. The final sample consisted of 150 CBCTs, including 91 females and 59 males, with ages ranging from 13 to 89 years (mean age of 47.06; ± SD=18.722), which presented an accumulation of 178 dental inflammations. The gender, age, presence and location of dental inflammation as well as presence and location of MCB were recorded. The Kolmogorov-Smirnov, Chi-square, and T-test were applied to verify the statistical relationship of the data.

RESULTS: There were 178 images of dental inflammation on the 150 CBCTs, mainly located at molars' region (75%). The apical lesions were the most common type of dental inflammation found (79 or 44.4% of the sample), followed by pericoronitis (32; 18.0%). This study identified 135 mandibular canal branches in the regions that presented dental inflammation. The MCB were also most commonly located at molars' region (74.07%). The MCB found were mostly single (86 or 63.7% of the total). The most common direction of the branches after arising from the mandibular canal was toward upper region (126 or 93.4%). Gender had no influence on mandibular canal branching (p=0.308), not did age (p=0.728). No statistical difference was identified regarding the distribution of mandibular canal branching in relation to the sites with dental inflammation (p=0.370).

CONCLUSION: A high prevalence of mandibular canal branching was observed in the regions where dental inflammation was identified, most commonly found in the molar region.

Key Words: Mandible; inferior alveolar nerve; mandibular canal; bifid mandibular canal; cone beam computed tomography.

Core Tip: The identification of MCB is important for the success of several dental procedures. Neurovascular structures derived from the inferior alveolar nerve were found within MCB. Painful symptoms and difficulties with anesthetic procedures are increased on mandibular alveolar ridges affected by dental inflammation, but the phenomena involved remains not clear. The occurrence of neurovascular anatomical variations is considered as a possible causal factor. It has been difficult to determine the true role of the inflammation in relation to supplementary innervation in these situations. The purpose of the present study was to search for some evidence of such phenomenon in mandibles.

Audio Core Tip

INTRODUCTION

Neurovascular branching in the mandibular region is a variation of normality and may occur with the mylohyoid and the inferior alveolar nerves. The inferior alveolar neurovascular bundle is the main responsible for the innervation and blood supply to mandibular structures. This bundle enters into the mandibular canal, an intraosseous duct usually unique in each hemi-mandible[[1-3]].

Variations of the mandibular canal pathways, commonly named bifid or trifid canals, were related to embryonic malformations[4]. Their location and prevalence vary depending on the type of diagnostic test used. On panoramic X-rays, these were mainly located in the ramus region, with prevalence reports varying from 0.08% to 16.8%. When using three-dimensional (3D) images, these were also found in the posterior region, with a higher prevalence ranging from 9.8% to 65%[1,5-12].

Classifications of this anatomical landmark were performed based on two-dimensional (2D) exams[1,5-6]. Once 3D imaging has presented a higher sensitivity and specificity in detecting/identifying mandibular canal branches (MCB), other descriptions and classifications were proposed[7-12]. Regardless of the method, the classifications are usually related to location, number, and direction of the MCB[5-6,12].

Fukami et al. (2012)[13] found neurovascular structures derived from the inferior alveolar bundle present within MCB; therefore, these structures may well be related to sensory alterations in mandibles. In this sense, it is important to know the anatomy of the mandibular canal and its anatomical variations. The identification of these structures is important for the success of dental procedures, such as implant placement, extraction of impacted teeth, apical surgeries, bilateral sagittal split osteotomies, and pathology enucleating[14-19]. There are reports of a relevant prevalence of postoperative neuropathic pain due to inferior alveolar nerve injuries during surgical procedures[14,20].

In addition, call attention that painful symptoms and difficulties with anesthetic procedures are increased on mandibular alveolar ridges affected by dental inflammation[21-23]. Besides the endogenous inflammatory factors related to pain, one hypothesis is referred to the occurrence of anatomical variations of the nerves responsible for mandibular sensitivity[3,20-24]. It has been difficult to determine the true role of the inflammation in relation to supplementary innervation in these situations[3,21-22-24]. Clinical interaction between dental inflammation and nerve alterations was identified even when the inflammation site was relatively far from the neurovascular alteration, but the phenomena involved are still not clear[21].

The influence of inflammatory mediators on dorsal root regeneration of spinal cords of rats and neurogenesis in human intervertebral discs were already observed by Di Maio et al. (2011)[25] and by Lee et al. (2011)[26]. The purpose of the present study was to search for some evidence of similar phenomena in mandibles. The mandibular canal was assessed in alveolar ridges affected by dental inflammation using a large sample of CBCT at two different oral radiology centers from Brazil and Canada. An evidence of association between dental inflammation and MCB can be useful for improving the knowledge about inflammatory effects in mandibles, avoiding neurovascular injury during surgical dental procedures in alveolar ridges affected by dental inflammation, by previewing the occurrence of this anatomical variation. Besides that, it will stimulate the search for the inflammatory mediator responsible for stimulating such neurovascular response.

MATERIALS AND METHODS

Approval in research ethics from the Federal University of Minas Gerais (UFMG) (Brazil - COEP 432.2982) and the University of Alberta (Canada - Pro00050422), including informed consent from each patient, were obtained for the present study. Mandibular CBCTs were obtained from the database of a private diagnostic imaging center (Hermes Pardini Institute - Belo Horizonte, Brazil) and from the University of Alberta's Department of Dentistry database. These images were taken for diagnostic and medical purposes, as requested by the patients' clinicians. This study assessed a set of 2,484 CBCTs, 1,307 from the Brazilian and 1,177 from the Canadian centers.

CBCTs were obtained from I-CAT® (Next Generation Model – Imaging Sciences International – Hatfield, PA, USA). The Brazilian scans were acquired using a voxel size of 0.25 mm, a field of view of 7x16 cm, and an exposure time of 26.9 seconds (120kV; 3-7 mA). The Canadian scans were acquired with a voxel size of 0.3 mm, a field of view of 13x16 cm, and an exposure time of 8.9 seconds (120kV; 3-7 mA). The images were analyzed by creating panoramic views (5.25 to 10.25 mm in thickness) and multiplanar sectional slices (1 mm in thickness and 1 mm in spacing), using the Xoran® software (Xoran Technologies - Ann Arbor, MI, USA). Different voxel sizes were due to different clinical requirements for imaging. The T-test for independent samples was used to verify their diagnostic accuracy of mandibular canal branching. The result showed a homogeneity of variance that was statistically significant (p=0.122). Thus, the different voxel sizes had no influence on the detection of MCB.

Assessments were performed by an oral and maxillofacial radiologist (MAAC), specialist with 12 years of experience, using a 20” LED monitor with a 1600 x 900 pixel resolution (Flatron E2442TC model - LG Electronics – Seoul, South Korea). Intra-examiner reliability was performed analyzing 20 randomly selected CBCTs three times, with 15 day intervals between each evaluation trial. The Kappa test was used to determine intra-examiner reliability, and almost perfect agreement for the detection of the ramifications was found (.842)[27].

The 2,484 CBCTs were analyzed for the presence of dental inflammation in the mandibular posterior region of the alveolar ridge, at the molar and premolar regions. The detection of dental inflammation was performed along with the review of the clinical charts of the patients who had CBCTs taken. The dental inflammations were confirmed in the CBCTs and were considered to be 1) bone lesion-like radiolucency located adjacent to the root tips and with endodontic origin; 2) osteolysis surrounding the roots, which represented combined periodontal and endodontic lesions; 3) vertical and/or horizontal bone loss, which represented typical periodontal disease; 4) osteolysis surrounding implants, which represented diagnoses of the peri-implantitis; 5) sites of external inflammatory root resorption, concomitantly with adjacent radiolucency, suggesting osteolysis; 6) a thickening of the periodontal ligament space, presenting an additional sign of pericementitis, and/or 7) a thickening of the pericoronal region of the impacted teeth, presenting an additional sign of pericoronitis.

The following variables were recorded in a spreadsheet: gender, age, presence and location of dental inflammation, and mandibular canal branching. Age was dichotomized by its median in order to verify whether or not there would be differences between mandibular canal branching and the age groups (younger or older individuals). The location of dental inflammation and mandibular canal branching was determined in the ramus, as well as in the retromolar, molar, or premolar regions. In cases of periodontal disease with horizontal bone loss, the entire mandible was considered to be the location. The MCB location was defined as the site where the branches emerged from the mandibular canal. The total number of MCB in each patient and the occurrence of contact between the dental inflammation and the branches were also analyzed.

According their features, the MCB were classified as: 1) number: single, double, or multiple, considering their number after arising from the mandibular canal; 2) orientation: upper, inferior, vestibular, or lingual, according to their direction after arising from the mandibular canal; 3) connection with dental inflammations: when terminations had contact or not with the dental inflammation; and 4) classified according with the location of connection with dental roots on apical, medium, or cervical thirds.

The statistical analysis was performed by one of the authors (MHGA), an biomedical statistician, using the Statistical Package for Social Sciences (SPSS - 21.0, IBM, Armonk, NY, USA), with the significance level set to 5% ($P < .05$). The Kolmogorov Smirnov test was used to verify the distribution of the sample, and the T-test, Chi-square test, or Fisher Exact tests were used to assess the statistical differences between the occurrence of the MCB and the variables.

RESULTS

This study identified 150 patients that presented dental inflammation, of whom 46 were Canadians and 104 Brazilians; 91 females and 59 males, with ages ranging between 13 and 89 years (mean age of 47.06; ± SD=18.722). The final sample consisted of 178 images of dental inflammation, taking into account both sides of each patient. Twenty-four patients presented two images of dental inflammations, and one patient presented three images; 75.3% of the dental inflammation was found in the molars region and 24.7% in the premolar region.

There were 135 MCB among the 178 images that presented dental inflammation (75.8%). No statistically significant difference was found regarding gender ($p = 0.308$) and mean age ($p = 0.077$) for the occurrence of the branches. The sample's median age was 50 years; 50.37% of the MCB occurred in patients of up to 50 years of age and 49.63% in older patients. The T-test showed that the homogeneity of variance of the MCB when comparing the groups was statistically significant ($p = 0.728$).

The MCB was most commonly located in the molar regions (74.07%). The premolar regions presented 22.2% of the branches (Table 1). No statistically significant difference between the location of the occurrence of MCB and the dental inflammation was observed (Table 2).

The MCB found were mostly single (86 or 63.7% of the total). There were also 28 double branches (20.7%) and 21 multiple branches (15.6% of the total). The most common direction of the branches after arising from the mandibular canal was toward upper region (126 or 93.4%) (Figures 1A and 1B). This study also found three branches stemming in the lingual direction (2.2%) and three in the vestibular direction (2.2%), as well as and three toward the posterior region (2.2%) (Figure 2). Considering the 135 exams that presented MCB, the number of branchings and their directions were compared. No difference between the frequencies of the number and the directions of the MCB were observed ($p = 0.608$) (Table 3).

This study found that 97 MCB (71.8%) were connected with dental inflammation. This finding represented 54.5% of the dental inflammations. The connections were located on the apical third of the roots (37.0%) (Figure 1B), on the medium third (20.0%) (Figure 1A), or on the cervical third (14.8%) (Figure 2); 28.2% of the MCB did not come into contact with dental inflammations.

When analyzing only the exams with MCB, the apical lesions (Figures 1A and 1B) were the most common type found (59 or 43.7%), followed by pericoronitis (29 or 21.5%). Combined endodontic-periodontal lesions were the third most common and were present in 20 scans (14.8%). There were also 13 cases (9.6%) with periodontal bone loss, 10 cases (7.4%) with signs of pericementitis, 03 cases (2.2%) presenting perimplantitis (Figure 3), and 01 with inflammatory root resorption (0.7%).

DISCUSSION

To observe if there would be some alteration of the mandibular canals in mandibles affected by dental inflammation, the present study assessed 2,484 CBCTs. The main finding of this study was the high prevalence of MCB in the same regions where there were dental inflammations, without statistically significant differences. This is a novelty since any previous study has considered a post natal physiologic process, such as inflammatory dental lesions, as a variable related with MCB.

The dental inflammations were mainly found in the molar region with apical lesions representing the most commonly found type of inflammation. These findings are in accordance with Awad et al. (2013)[28], who identified apical cysts and granulomas as the most common lesions affecting the jaw, with the largest proportion located in the posterior regions.

No statistically significant differences of the occurrence of MCB could be observed with patient age or gender. This finding is in accordance with that reported by Nortjé et al. (1977)[5], who also found no correlation between MCB and with patients or gender after having evaluated 3,612 panoramic radiographs. Similar results were also observed in studies that assessed MCB in CBCT exams, although these did not consider dental inflammation as a variable[12,29].

The MCB were mostly single and directed to the upper region. These branches appear to be similar to the dental branches described by Naitoh et al. (2009)[12], but this 3D classification was not used in the present study, given that the identified branches were not usually directed toward the root tips, as reported in Naitoh et al.'s (2009)[12] work. The single and upper branches often ran in the direction of different thirds of the roots and came in contact with dental inflammations. In addition, there were also other different patterns, such as double or multiple branches, some posteriorly oriented or directed toward non-dental inflammatory lesions, such as peri-implant lesions.

Regarding the previous 2D classifications, it is important to consider an additional issue about the location of the branches. Most of MCB found in the present study emerged in the posterior region of the alveolar ridges, named as molar or premolar regions, near dental inflammations. Since the classifications for mandibular canal branching based on panoramic radiographs were referred to bifid canals that emerged within the ramus, these classifications were not adopted in the present study[5,6].

A large number of MCB were linked to dental inflammations. This finding reinforces the suspicion of a relationship between supplementary innervation and dental inflammation[3,24] and can be combined with existing evidence supported by scientific bases that prove this possibility[25,26]. Since other studies on bifid mandibular canals did not consider any post natal physiologic processes, such as the inflammatory response[5-13], their findings could not be used to compare the peculiar occurrence, location, and aspects of the MCB identified in this study.

One issue that could arise would be the possibilities of the MCB containing only blood vessels, as a result of the vascular phenomena involved in inflammatory response. Although vascular alteration can be also considered a potential risk for surgical procedures, Neves et al. (2010)[9] stated that the imaging assessment of MCB assumes the presence of the inferior alveolar neurovascular bundle, due to its origin. Confirming this statement, the histological investigation of Fukami et al. (2012)[12] detected that branches include both vascular and neuronal components.

The occurrence of the supplementary innervation of the inferior alveolar nerve is considered a hypothesis for increased painful symptoms and difficulties with the anesthetic procedures of alveolar ridges affected by dental inflammation[3,21-24]. In this sense, adding this question to the surgical risk of neurovascular injuries, the occurrence of MCB must be considered by clinicians when planning surgical procedures on mandibles that have been previously affected by dental inflammations, in order to avoid neurovascular damage and to optimize anesthetic procedures.

According to the American Academy of Oral and Maxillofacial Radiology, among others, the CBCT exam is currently the main imaging modality for detecting mandibular canals and their variations[7-13,30]. The diagnosis of this important anatomical structure is crucial when planning several dental procedures, including implant insertions, apical surgeries and other endodontic procedures, extractions of non-erupted teeth, as well as other surgical procedures[14-19]. As the CBCT is highly sensitive, it is clear that the detection of MCB was not affected by the method used in this study.

Therefore these branches may well be related to inflammatory phenomena, our study presents a limitation, which refers to a possible detection of preexistent branches that have not been previously detected or classified. It means that the MCBs found in this study may be a kind of preexisting canal, and their detection at the same site of dental inflammation may be a coincidence. Nevertheless, no prior description of these MCB has been adequately presented in the literature, as well as such high simultaneous prevalence of MCB and dental inflammation.

Thus, the high prevalence of MCB at the same regions with dental inflammations, as well as their proximity, are a phenomena no previously detected, that are similar and in accordance to those found by Di Maio et al. (2011)[25] and Lee et al. (2011)[26]. This can help to explain the higher sensitivity of mandibles affected by inflammation and also open new perspectives for additional research on a possible relation between neurovascular alterations and inflammation. Epidemiological research, such as case-control and longitudinal studies, in addition to molecular studies about the action of endogenous factors, can provide further information on their origin and relationship.

CONCLUSIONS

A high prevalence of mandibular canal branching was observed in regions that presented dental inflammation, most commonly in the molar regions.

COMMENTS

Background

The inferior alveolar neurovascular bundle is the main responsible for the innervation and blood supply to mandibular structures. It enters into the mandibular canal, an intraosseous duct usually unique in each hemi-mandible. MCB is a common morphological variation. Its location and prevalence vary depending on the type of diagnostic test used. The 3D exams have found higher prevalence of MCB, ranging from 9.8% to 65%. It is important to know the anatomy of the mandibular canal and its anatomical variations, considering the increased risk of neurovascular injury related the high MCB prevalence. Although MCB has been related to embryonic malformation, clinical interaction between dental inflammation and nerve alterations was identified even when the inflammation site was relatively far from the neurovascular alteration[21]. Once the phenomena involved with these situations are still not clear, the present study aimed to assess the MCB in regions with dental inflammation.

Research frontiers

Sensitivity and difficulties with anesthetic are increased on mandibles affected by dental inflammation, even when compared to maxillary teeth. Besides the endogenous inflammatory factors, one hypothesis is referred to morphological variations of the nerves[3,20-24]. It has been difficult to determine the true role of the inflammation in relation to supplementary innervation.

Innovations and breakthroughs

Neurogenesis was already observed and related to inflammatory phenomenon[25-26].

Applications

The purpose of the present study was to search for some evidence of similar phenomena in mandibles that can help to improve the predictability of MCB by clinicians and support research for some therapy for neurovascular damage.

Terminology

Mandibular canals variations have been usually named as bifid or trifid canals by several authors. They are mainly referred to those double canals located at ramus region. Once higher variability of this alteration was already found, some of them without adequate description and classification in the literature, the denomination mandibular canal branching (MCB) seems to be more appropriated.

Tables

Table 1 – Distribution of mandibular canal branches per region (N=135)

	Branches						
	Right side			Left side			
	Ramus / Retromolar	**Molar**	**Premolar**	**Premolar**	**Molar**	**Ramus / Retromolar**	Total
Number (%)	02 (1.5%)	52 (38.5%)	17 (12.6%)	13 (9.6%)	48 (35.6%)	03 (2.2%)	135 (100%)

Table 2 – Distribution of mandibular canal branching in relation to locations of the dental inflammation

Location of dental inflammation	**Mandibular canal branching**		**P value***
	No	**Yes**	
Premolars	6 (16.7%)	30 (83.3%)	
Molars	34 (25.4%)	100 (74.6%)	0.370
Ramus/Retromolar	3 (37.5%)	5 (62.5%)	

* Pearson Chi-square Test

Table 3 – Distribution between locations of dental inflammations and mandibular canal branches

Direction of the Mandibular canal branching	**Number of mandibular canal branching**		**P value***
	Single	**Double or multiple**	
Lingual	3 (100%)	0 (0%)	
Superior	80 (63.5%)	46 (36.5%)	
Vestibular	1 (33.3%)	2 (66.7%)	0.608
Posterior	2 (66.7%)	1 (33.3%)	

* Fisher Exact Test

Figures

Figure 1 - 1A: Single, superior and medium third mandibular canal branch toward apical lesion of tooth 35 (white arrows); 1B: Single, superior and apical mandibular canal branch (white arrows) toward apical lesion of tooth 35.

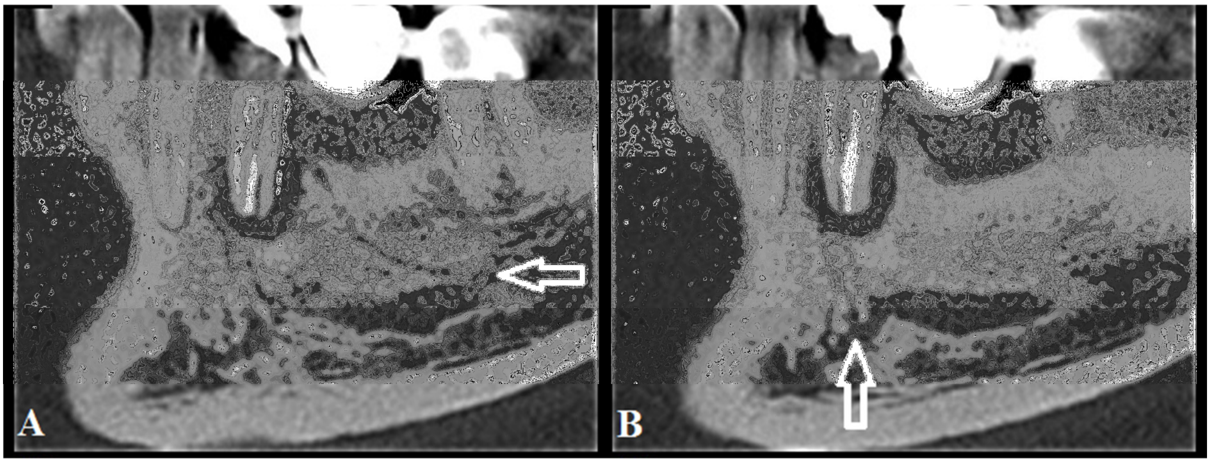


Figure 2 – Single, posterior and cervical mandibular canal branch (white arrow) to a horizontal bone loss.

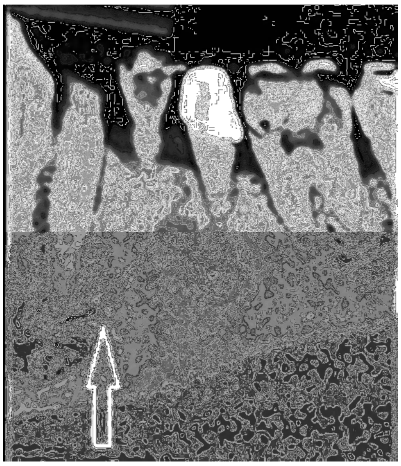
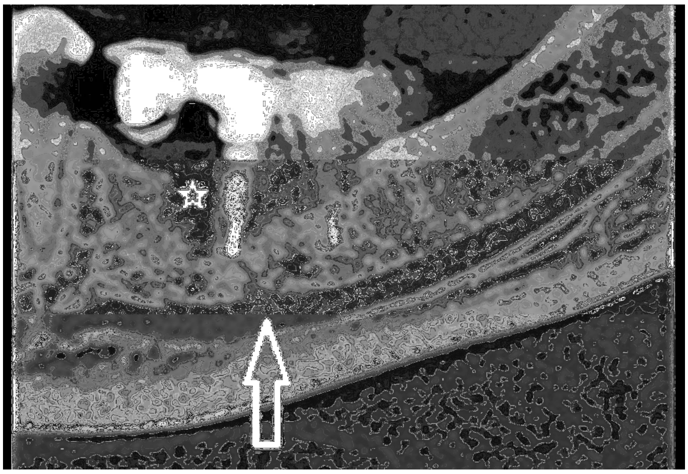


Figure 3 - Perimplantitis surrounding implants (white star) and double, superior and apical mandibular canal branch toward perimplantitis (white arrow).



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6.3 Artigo 3 – Submetido a “Surgical and Radiologic Anatomy”

TITLE: Mandibular canal branching assessed with cone beam computed tomography

RUNNING TITLE: Mandibular canal branching in CBCT

KEYWORDS: Inferior alveolar nerve; mandibular canal; bifid mandibular canal; dental radiography; cone-beam computed tomography.

Original article

Mandibular canal branching assessed with cone beam computed tomography

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Abstract

Purpose: The mandibular canal must be considered in dental procedures to avoid injuries of the alveolar inferior nerve. The occurrence of anatomical variations of the mandibular canal increases the risk of neurovascular injuries. The purpose of this study was to identify and describe the prevalence of mandibular canal branching (MCB) using cone-beam computer tomography (CBCT).

Methods: Seven hundred standardized CBCTs were selected. The images were evaluated for the presence of MCB and for the detection of pathologies that could affect the structure of the canals. The data were analyzed using descriptive statistics and the chi-square test.

Results: The prevalence of MCB was 41.1%. There was no statistical difference between genders with the presence of the branches ($p>0.005$). The highest prevalence was in the premolar and retromolar regions. Pathologies found in the molar region were frequently connected with MCB (77.8%), and the most common pathology related to branches was periapical lesion.

Conclusions: Mandibular canal branching presented a high prevalence in CBCT imagery, more frequently located in regions of the premolar and retromolar. An adequate diagnosis of the MCB is necessary to perform dental procedures and verify possible associated pathologies.

Key Words: cone beam computed tomography; mandibular canal; mandible; inferior alveolar nerve; bifid mandibular canal.

Mandibular canal branching assessed with cone beam computed tomography

Introduction

The mandibular canal is an important anatomical structure to be considered in dentistry, and branching has been reported in prior literature [12,18,21]. It is necessary to understand its anatomy in order to avoid injuries of the alveolar inferior neurovascular bundle, such as peri-implant fibrous tissue formation, sensory disturbances, traumatic neuroma, or bleeding [5,7,11,16,19,20,28]. The origin of mandibular canal branching (MCB) is related to failure of the primitive canal fusion occurring in the pre-natal period [4]. Studies have reported no difference in gender and age in the occurrence of MCB [6,11,24], while others have found a higher prevalence of bifid canals in males [8,20].

The location and prevalence of MCB is variable depending on the type of diagnostic method. Prevalence on two-dimensional exams is reported from 0.08% to 16.8% [7,10,13,20,23]. When using three-dimensional (3D) images, MCB presented a prevalence from 9.8% to 65% [8,11,16,20,21].

Although Mizbah et al. [19] and Neves et al. [22] have considered two-dimensional imaging as having good diagnostic accuracy for detecting MCB, there was no diagnostic agreement between panoramic radiographs and computed tomography [20,29]. Kim et al. [13] showed that panoramic radiographs do not have a good specificity in identifying MCB. Other studies have demonstrated that 3D imaging is more adequate to detect MCB and analyze their characteristics, such as locations and direction, as well as whether they are unilateral or bilateral [5,9,16,21,28]. It has been stated that the improvements provided by 3D imaging make it possible to find branches not yet identified [3,18,28].

The large number of procedures performed in the posterior region of the mandible implies that the mandibular canal deserves attention from clinicians. The anatomical variations of the mandibular canal must be considered as an important anatomical structure in the surgical planning of the procedures, such as implant insertions, extractions of included teeth, biopsies, enucleations and curettage of pathologies, apical surgical interventions, harvesting of block bones, as well as anesthetic procedures [10,11,12,16,18,21,28]. Thus, considering the higher diagnostic accuracy of CBCT in identifying and depicting MCB, the purpose of this study was to identify and describe the prevalence of this mandibular canal alteration in a Canadian sample consisting of patients who received dental care at the University of Alberta.

Material and Methods

Ethics approval was obtained from the University of Alberta for this study (Pro00050422). The Department of Dentistry database was used to collect the sample to assess mandibular canals and to identify MCB. One thousand one hundred seventy-seven CBCTs were evaluated. The CBCT examinations were requested by clinicians to aid in the diagnosis and treatment planning for the respective patient's needs.

CBCTs were obtained from an I-CAT® (Next Generation Model – Imaging Sciences International – Hatfield, USA), with a field of view equal to 13 x 16 cm, 0.3 mm voxel, and 8.9 seconds of exposure time. As the main clinical reasoning for the examinations was due to orthodontic recommendations, the CBCTs included had a large field of view and a voxel size of 0.3 mm.

CBCT images were analyzed by creating panoramic views (5.25 to 10.25 mm thickness) and multiplanar sectional slices (1 mm thickness and 1 mm spacing), using Xoran® software (Xoran Technologies - Ann Arbor, USA). Examinations that did not show the entire mandible or that presented artifacts derived from patients' movements were excluded.

Assessments of images were performed by an oral and maxillofacial radiologist (MAAC), a specialist with 10 years experience, using a 20" LED monitor with 1600 x 900 pixel resolution (Flatron E2442TC model - LG Electronics – Seoul, South Korea). Intra-examiner reliability was performed by analyzing 20 randomly selected CBCTs three times with 15-day intervals between each evaluation trial. The Kappa test found almost perfect agreement of the intra-examiner in the detection of MCB (0.842) [17].

The variables analyzed were: gender, occurrence of MCB located between the mandibular foramen and mental foramen, pattern of occurrence (number of branches in each patient), region of MCB origin (ramus, retromolar, molar, premolar, or mental foramen), presence and localization of foramina at the end of the branches, location of the foramina, images of pathologies located between the mandibular foramen and mental foramen, connection between MCB and pathologies, kind of pathology connected to MCB, and region of connection between MCB and pathology. The variables were recorded on a spreadsheet.

The number of branches was referred to the total number of branches that emerged from both sides of each patient: single - one branch – or multiple – two or more branches. The location of MCB was defined as the site where the branches emerged from the mandibular canal. The branches that emerged between the mandibular foramen and the anterior edges of the ascending ramus were considered ramus branches. The branches toward the region between anterior edge of the ascending ramus and the distal surface of the third molars were considered retromolar branches. The molar and premolar branches were defined as those located below the corresponding teeth. The branches that emerged from the mental foramen region were considered to be mental foramen branches.

When MCB emerges in its own foramen, which is not the mental foramen, the secondary foramen were called foramina. The locations of the foramina were on the vestibular or lingual plates or on the occlusal surface of the alveolar bridge. When located in the premolar region, they were defined as secondary mental foramina, since they were not the mental foramen, the main foramen in this region.

The tomographic images of evaluated pathologies were 1) pericoronitis: thickening of the pericoronal follicle of the impacted teeth; 2) apical lesion: hypodense area adjacent to root tips); 3) periodontal – endodontic lesion: osteolysis surrounding the roots, whether or not associated with vertical or horizontal bone loss; 4) cystic lesions: dentigerous or paradental cysts; 5) osteitis/osteosclerosis/enostosis: increased density of the bone marrow; 6) peri-implantitis: hypodense area surrounding dental implants, whether or not associated with vertical or horizontal bone loss; and 7) periodontitis: vertical or horizontal bone loss, beyond biological bone remodeling (2mm) [23-24]. This study verified if in fact some MCB came in contact with the tomographic images of the pathologies. If present, the kind of pathology connected to MCB was recorded.

A statistical analysis was performed using the Statistical Package for Social Sciences (SPSS - 21.0, IBM Akron, USA), with the level of significance set to 5% ($p<0.05$). The Kolmogorov-Smirnov and chi-square tests were used to verify the distribution of the sample, compare the sides of each patient, and evaluate associations of MCB with other variables.

Results

After evaluating the database, 700 CBCTs were included in the study (279 male and 421 female; mean age = 20.97 years; median = 16 years). 288 CBCTs (41.1%) presented MCB (Figure 1). When analyzing the 288 CBCTs with MCB, a total of 425 branches were identified. Among them, 177 (61.5%) presented one branch (Figures 1, 2, and 3). One hundred eleven exams (38.5%) presented more than one MCB (Figures 1 and 4A).

Fig. 1 Flow chart - exams of the 1177 cone beam computed tomography

Fig. 2 Single MCB in molar region (white arrow) toward apical lesion (white stars)

Fig. 3 Single mandibular canal branching in retromolar region (black arrows) with foramina (white arrow)

Fig. 4 (a) Multiple MCB in the retromolar region at the same side of the mandible. Black arrows: a ramus branch. White arrows: a retromolar branch with foramina; (b) Gray arrow (axial slice): a single lingual premolar MCB with foramina in the same patient

Considering the sides that were affected, 67.4% of the patients with MCB presented unilateral branches (194 patients - 69 male and 125 female) and 32.6% had branches on both sides (94 patients - 37 male and 57 female). Seventeen cases (8.72%) were found to have multiple branches affecting the same side, including one case with three branches and another with five. There was no statistical difference of gender with the presence of MCB or with the pattern of occurrence (unique or multiple) ($p>0.05$).

Locations of MCB are reported in Table 1. The branches were distributed as follows: 56.5% on the right side and 43.5% on the left side. Considering both sides, the premolar region presented the highest prevalence (188 – 44.2% of the sample) (Figure 4B). The second most affected region was the retromolar region (108 individuals – 15.42% of the sample (Figure 3).

Ninety-two percent of the premolar branches ended in foramina, with the most common location found on the lingual surface of the mandible (93.1%) (Figures 3B and 4). There was also a high prevalence of foramina among the retromolar branches (70.4%). No difference was observed in the occurrence of MCB located in the premolar region with the occurrence of foramina at the same region ($p>0.05$).

There were 71 CBCTs with MCB in the ramus region, most of which had no foramina (76.1%). When present, the most common location of the foramina was on the lingual surface (11.3%).

Among the 700 CBCTs, 58 exams presented at least one tomographic image of pathology. When studying only individuals with MCB, 45 tomographic images of pathologies were detected (Table 2). The most common was apical lesions, present in 15 (33.3%) cases.

When comparing the presence of tomographic images of pathologies and MCB per region, the coexistence of tomographic images of pathologies and MCB in the molar region was commonly found (Figure 2). There was a statistically significant difference ($p<0.05$) between MCB and pathologies in this region, which was not observed in the other regions (Table 3).

Twenty-five tomographic images of pathologies were connected to MCB. Fourteen pathologies were connected with MCB located in the molar region. Apical lesions represented the pathology that was more frequently linked with MCB, with connection detected in 8 exams. The second most frequent lesion was pericoronitis in 7 cases.

Discussion

Mandibular canal branching has presented a prevalence ranging from 0.08% [23] to 65% [11], depending on the diagnostic tool used. In the present study, the amount of MCB found from the total analyzed sample (41.1%) falls within that range. This result is similar to a previous study by Muinelo-Lorenzo et al. [20], also conducted using CBCTs, which reported a prevalence of 36.8% of MCB from a total of 225 examinations. The authors compared panoramic radiographs and CBCTs used to detect MCB and found that 3D exams presented a higher sensitivity [20].

In addition, Kim et al. [13] and Sanchis et al. [29] stated that panoramic radiographs do not present a good specificity for identifying MCB. Furthermore, Fukami et al. [9] detected that CBCTs have a good specificity for this goal through histological evidence. Thus, based on these findings, it can be concluded that the findings obtained by CBCTs are reliable, since this method is able to improve detection and show the features of the mandibular canals and their variations, as compared to 2D exams [5,16,21.28].

The occurrence of MCB was not related to gender. Although this result is different from the findings of Fu et al. [10], which found a statistical association with males, it is in accordance with the majority of studies that have also found no difference with respect to gender [6,11,21,24].

Regarding the affected sides, most of the MCB found were unilateral. Regardless of the number of affected sides, when considering the total sample, females presented more cases of MCB. When considering the proportion of the genders in this sample (60.1% female and 39.9% male), both had a similar prevalence. Hence, the larger number of females, when compared to males, with MCB is due to their higher proportion in the sample.

Regarding the cases with multiple branches affecting the same side of each patient, Muinelo-Lorenzo et al. [20] reported a similar percentage of unilateral double branches (7.2%) among exams with MCB. Comparing unilateral and bilateral findings, the high prevalence of unilateral MCB (67.4%) is not in accordance with Nortjé et al. [23], which observed a higher prevalence of bilateral bifid canals in their 2D radiographs.

The higher number of unilateral MCB raises doubts about its etiology. Chavez-Lomelí et al. [4] supposed mandibular canal alterations as a malformation derived from a systemic action of a prenatal factor disturbing the fusion of three separate prenatal canals. If the prenatal malformation theory is correct, the causal factor may act simultaneously on both sides, in most cases. But this theory was proposed based on an evaluation of a sample that included only hemimandibles and could not be compared with the present findings. The high number of unilateral MCB found in the present study does not permit the confirmation of a systemic effect from a prenatal factor and opens a new perspective about the influence of a local postnatal causal factor.

A higher number of MCB has emerged from the mandibular canal in the premolar region. The second most prevalent region was in the retromolar region. The prevalence of retromolar MCB is in accordance with Muinelo-Lorenzo et al. [20], which found a similar percentage (12.0%) in their sample. Unlike our findings, Orhan et al. [24] reported no premolar branches and found retromolar branches to be the most common MCB.

The branches detected in the premolar region were frequently toward the lingual region and had a high prevalence of lingual foramina. It is hypothesized that the MCB along the foramina located in the premolar region can be related to branches of the mylohyoid nerve. Since some anatomical studies have shown that this nerve has branches entering the mandible through the lingual surface, including the premolar region [2,15,27,30], premolar branches may represent an evidence of the supplementary innervation from the mylohyoid nerve, forming an anastomosis with the inferior alveolar neurovascular bundle, according to Krasny et al. [15]. In this way, the occurrence of premolar MCB could help explain difficulties with anesthetic procedures [10].

The most common tomographic image of pathology found overall was apical lesions. This result was expected, since granulomas and cysts are the most common lesions affecting the maxilla and the mandible [1]. The simultaneous occurrence of a large number of pathologies and MCB is an important finding. This happened in a pronounced way in the molar region, where most of the pathologies were in contact with MCB, and represents an additional reason for the suspicion of a local action of a postnatal causal factor. It is suggested that pathologies may stimulate the delivery of endogenous factors that are able to trigger the growth of neurovascular tissues. This physiological mechanism has already been proven and may possibly occur in maxillofacial structures [14,25].

The large field of view and voxel size may have an effect on the identification of MCB, since these can vary in size. Although the multiplanar evaluation enabled by CBCT has allowed for the detection of MCB, smaller voxel sizes could hypothetically aid in the identification of smaller branches. Nevertheless, radiation is something that must be taken in account. Further studies should be performed on the factors that may influence or cause MCB, as this is an important anatomical structure to be considered in various procedures and anesthesia.

Conclusion

MCB had a high prevalence in CBCT examinations and were more frequently found in the premolar and retromolar regions. Adequate diagnosis of MCB is necessary to perform dental procedures and verify possible associated pathologies.

Conflict of Interest

The authors of the article “**Mandibular canal branching assessed with cone beam computed tomography”** declare that they have no conflict or interest regarding the study.

Tables

Table 1 - Regions with mandibular canal branching (MCB)

		MCB	
		N	**Percentage (%)**
Region	Ramus	71	16.7
	Retromolar	108	25.4
	Molars	55	13.0
	Premolars	188	44.2
	Mental foramen	03	00.7
Total		425	100.0

Table 2 – Tomographic images of the pathologies present in exams with mandibular canal branching

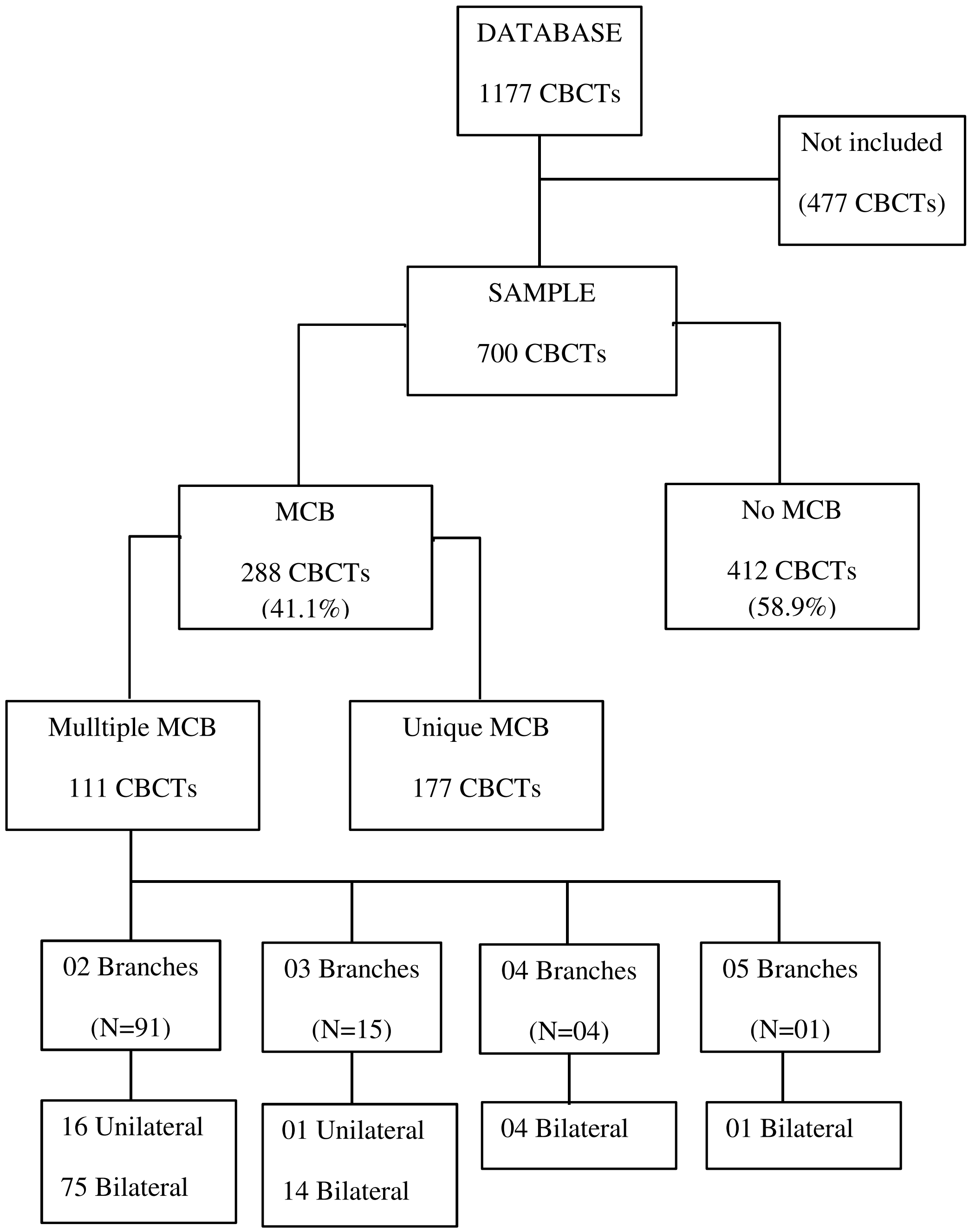
		Pathologies	
		N	**Percentage (%)**
	Pericoronitis	14	31.1
	Apical lesion	15	33.3
	Periodontal – endodontic	01	02.2
	Cystic lesion	03	06.7
	Osteitis/Osteosclerosis/Enostosis	08	17.8
	Residual roots	01	02.2
	Peri-implantitis	02	04.5
	Periodontitis	01	02.2
Total		45	100.0

Table 3 – Comparison of tomographic image of pathologies with mandibular canal branching per regions

		Tomographic images of the pathology			**P-value**	**OR**	**IC - (95%)**
		No	**Yes**	Total			
Region of mandibular canal branching	**Ramus**	71	00	71	< 0.01	17.077	9.600 – 30.376
	Retromolar	108	00	108			
	Molar	22	33	55			
	Premolar	176	12	188			
	Mental foramen	03	00	03			
	Total	380	45	425			

Figures

Figure 1. Flow chart - exams of the 1177 cone beam computed tomography.



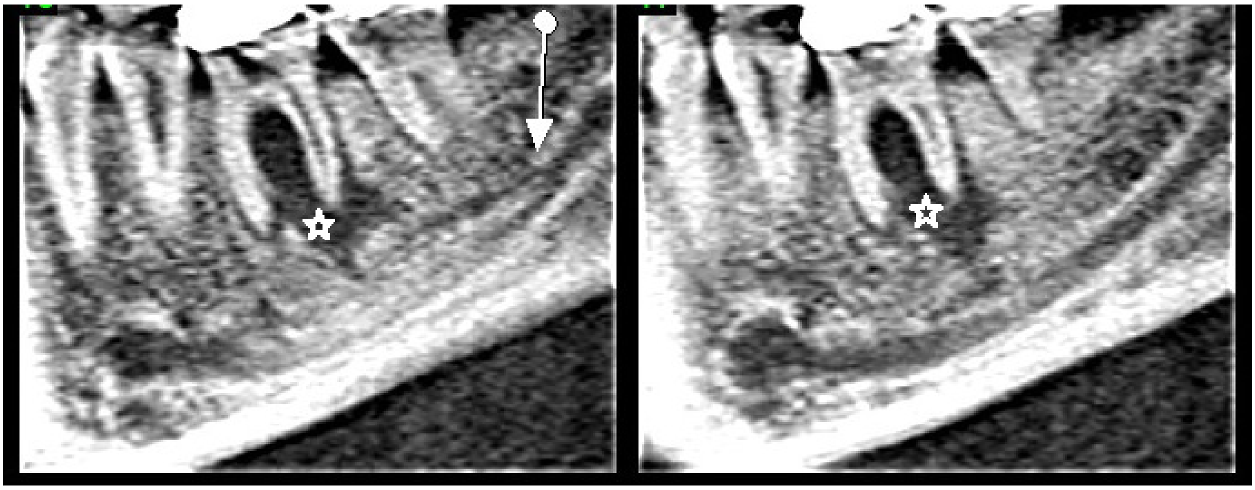


Figure 2: Mandibular canal branching in molar region (white arrow) toward periapical lesion (white stars)

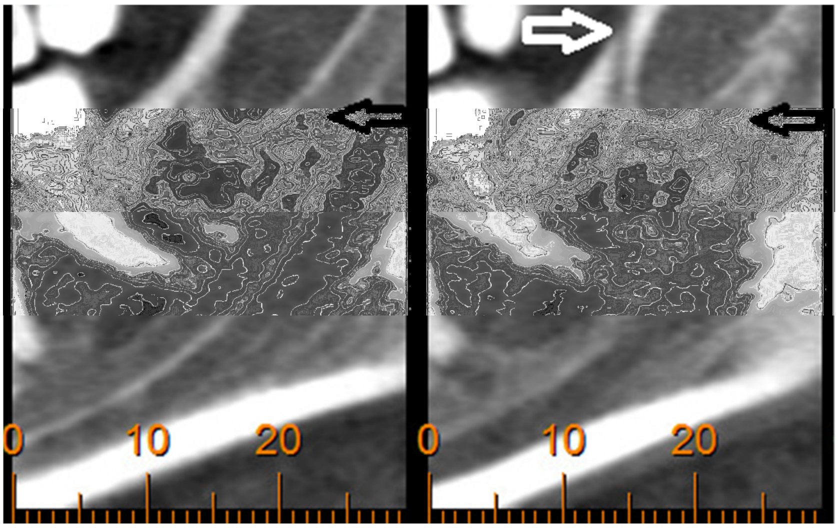


Figure 3: Mandibular canal branching in retromolar region (black arrows) with foramina (white arrow)

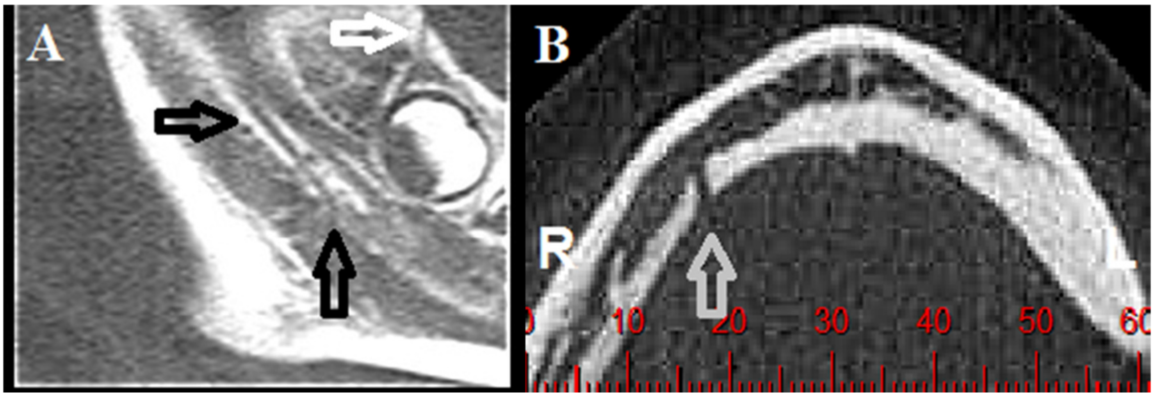


Figure 4: (A) Multiple MCB in the same side of the mandible as seen in a CBCT. Black arrows: a ramus branch. White arrows: a retromolar branch with foramina. (B) Gray arrow (axial slice): a lingual premolar branch with foramina.

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6.4 Artigo 4

TITLE: A case control study of mandibular canal branching and dental inflammation

RUNNING TITLE: Case control: mandibular canal branching and inflammation

KEYWORDS: Inferior alveolar nerve; mandibular canal; bifid mandibular canal; dental radiography; cone-beam computed tomography.

A case control study of mandibular canal branching and dental inflammation

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A case control study of mandibular canal branching and dental inflammation

Abstract

Purpose: to verify whether there is some relationship between mandibular canal branching (MCB) and dental inflammation.

Methods: the sample consisted of cone-beam computed tomography exams (CBCT) of 150 patients (50 cases and 100 controls), matched by age and gender, from two databases. The CBCTs were grouped considering the presence of MCB nearby the posterior teeth as the dependent variable. Dental inflammation and measurements of gray levels in the posterior region of the alveolar ridge were assessed on both groups, as independent variables. A multiple logistic regression analysis was applied to verify the relationship between MCB and the independent variables ($P<0.05$).

Results: the occurrence of dental inflammation increased the risk for MCB occurrence nearby posterior teeth ($P<0.001$; OR=11.640; CI-95% 4.327-31.311). Higher gray levels presented a weaker association with MCB ($P=0.002$; OR=1.002; CI-95% 1.002-1.003). The most frequent dental inflammation in both groups was endodontic (34 or 45.94% of the cases found). The dental inflammations mostly related to branches were endodontic (20 cases) and the combined endodontic and periodontal inflammation (20 cases), corresponding to 90% of the dental inflammations found in the case group.

Conclusions: There is association between MCB situated around the posterior mandibular teeth and dental inflammation. The dental inflammations of endodontic origin are most often associated with MCB.

Key Words: cone beam computed tomography; mandibular canal; oral pathology.

A case control study of the mandibular canal branching and dental inflammation

Introduction

It is established that dental inflammation presents painful symptoms [1,2]. Clinically, it has been reported to present special difficulty to anesthetic procedures, mainly when involving mandibular teeth [3,4]. It is unclear why inferior teeth are less susceptible to anesthesia comparatively to maxillary [4,5]. One hypothesis is referred to local alterations of the innervation [3-7].

The inferior alveolar neurovascular bundle is the main responsible for the innervation and blood supply of the mandibular structures. It lies into the mandibular canal, an intraosseous duct usually unique in each hemi-mandible. [8,9]. Morphological variations of the mandibular canals are supposedly related to embryonic malformations [10], but there are also reports of enlargements and growth of attached pathological masses related to pathologies [11,12].

Once there are reports of considerable postoperative neuropathic pain due to inferior alveolar nerve injuries [13,14], this anatomical landmark must be considered when treatment planning of dental implant placement, impacted teeth removal, apical surgeries, bilateral sagittal split osteotomy, biopsies, and anesthetic procedures [13-20].

The occurrence of morphological variations of the mandibular canals increases the risk of neurovascular damage by decreasing the predictability of neurovascular structures locations. It is necessary to identify these branches accurately, as well as their relationship with adjacent relevant structures. Histological evaluations have already proved the presence of inferior alveolar nerve branches inside MCB [10,20,21].

Two-dimensional imaging was the main diagnostic resource to identify the mandibular canal path. Prevalence and classifications of the MCB were reported mainly based on panoramic exams. There were reports of prevalence varying from 0.08% to 16.8%. The classifications were focused on MCB arising at ramus region [8,9,22,23].

Three-dimensional imaging enabled improvements on the identification of the canal morphology, with higher precision and accuracy [16,24-29], but reports of unknown morphologies and locations of MCB, according Langlais et al, create the expectation that it is still possible that there are branches not yet classified [23,29-34].

According Ritter et al. local conditions as the density gradient between hard and soft tissues can influence on quality diagnostic of anatomical structures. The gray level tool provided by the CBCT software has been used as a nonobjective indicator of this gradient density, contributing to elucidate this influence (kaya and Mah).

The present study found unclassified MCBs in the posterior region of the alveolar ridge, nearby dental inflammations, which have inspired the authors by raising the question on whether there is a relationship between MCB and inflammation. Similar situations were already detected in other structures of the human body [30-31]. Beyond explaining the increased sensitivity of mandibular teeth affected by dental inflammation, this relationship can be useful for decreasing the risk of neurovascular injuries during surgical procedures by improving the predictability of

MCB locations [3-4,46]. In this sense, the purpose of this case-control study is to identify MCB and verify if it present some association with dental inflammation.

Materials and methods

Ethics approvals, including informed consent from each patient, were obtained for the present case-control study by the Federal University of Minas Gerais-UFMG (Brazil-COEP 18263013.1.0000.5149) and by the University of Alberta (Canada - Pro00050422).

CBCTs of mandibles were obtained from the database of a private diagnostic imaging center (Hermes Pardini Institute - Belo Horizonte / Brazil) and from the database of the University of Alberta's Department of Dentistry. This study assessed a set of 2,484 CBCTs, 1,307 from Brazil and 1,177 from the Canadian center.

The exams were requested by clinicians for diagnostic reasons, as endodontic diagnostic, dental implant planning, orthodontic evaluation, and surgical planning of included teeth. The CBCTs scans were taken from I-CAT® (Next Generation Model – Imaging Sciences International – Hatfield, PA, USA). The scans acquired in Brazil were taken using voxel size equal to 0.25 mm, field of view equal to 7x16 cm, and 26.9 seconds of exposure time. The scans taken in Canada had 0.3 of voxel size, field of view of 13x16 cm and 8.9 seconds of exposure time. The different voxel sizes attended the clinical requirements for imaging.

The exams were analyzed by creating panoramic reconstructions (5.25 to 10.25 mm thickness), and multiplanar sectional slices (1 mm thickness and 1 mm spacing) using the Xoran® software (Xoran Technologies - Ann Arbor, MI, USA). The mandibles were evaluated for the presence of MCB arising from the mandibular canal.

Assessments were done by one of the researchers (MAAC), an oral and maxillofacial radiologist with 10 years of experience, on a 20” LED monitor with a 1600 x 900 pixel resolution (Flatron E2442TC model - LG Electronics – Seoul, South Korea).

Intra-examiner reliability and sample size calculation were performed assessing 20 CBCT scans randomly selected CBCTs (10 exams presenting MCB and 10 scans without MCB) for three times, with 15 days intervals between the evaluation trials.

The Kappa test was applied and found almost perfect agreement for diagnostic of MCB (k=0.842) [36]. These images were not included in the final sample.

T-test for independent sample was used for comparing the diagnostic accuracy of MCB on both databases. There was homogeneity of variance between them (*p*=0.122), indicating that the differences on voxel sizes had no influence on detection of MCB.

The sample size calculation indicated that a sample with 50 cases and 100 controls guarantees a test power of 99.9% and confidence level = 95% [37].

The CBCT’s were then divided into the groups:

1) Case group: 50 exams (23 males and 27 females; mean age = 50.88) presenting MCB arising from the mandibular canal in the region below the posterior teeth (molar and premolar regions);

2) Control group: 100 CBCTs (41 males and 59 females; mean age = 50.33) without MCB. Since non-branching canals have been reported to present higher prevalence [9,23,25,35], a proportion of two controls were obtained for every case found.

Age (KS=0.577; *P*= 0.893) and gender (KS=0.289; *P*=1.0) presented normal distribution, according to Kolmogorov-Smirnov test. The groups were matched for age (*P*=0.760) and gender (*P*=.0559), according to the *t*-Test and Chi-Square test, respectively.

Only one side of each patient was included in the final sample, in order to avoid alteration in the number of individuals of each group. In the case group, when there were branches on both sides, only one side was randomly chosen. In the control group just one side was randomly chosen for being evaluated as well.

The groups were then assessed and the following independent variables were recorded in a spreadsheet: presence and location of MCB, presence and location of dental inflammation, and bone marrow gray level at the posterior region of the alveolar ridge. The MCB location was defined as the site where the branches emerged from the mandibular canal in the posterior region of the alveolar ridge, considering the posterior teeth as the reference.

The dental inflammations recorded were 1) radiolucent image located adjacent to the root tips, of endodontic origin; 2) osteolysis surrounding the roots and extending to the alveolar crest represented combined periodontal and endodontic inflammation; 3) vertical and/or horizontal bone loss representing periodontal disease; 4) osteolysis surrounding implants representing absence of osseointegration (peri-implantitis); 5) sites of external inflammatory root resorption associated with adjacent osteolysis; 6) thickening of the periodontal ligament space, as an additional sign of pericementitis and/or 7) thickening of the pericoronal region of the impacted teeth, representing pericoronitis. In cases of periodontal disease with horizontal bone lost, the entire mandible was considered as the location.

The gray level was measured through the tool provided by the Xoran® software. The measurements were applied on sagittal slices, with 1 mm thickness, positioned along the path of the mandibular canals. The measurements were standardized with area equal to 4.71 mm^2 diameter, the smallest reproducible area in the evaluated exams, named as region of interest (ROI). In the case group the ROI was in the bone marrow just above the branches origin (Figure 1A). In the control group, the measurements were made just above the mandibular canal, and below to the mesial roots of the first molars (Figure 1B). The gray level values were dichotomized by the mean (593.793) and grouped as higher levels (greater than 593.793) or lower levels (up to 593.793), for comparison with MCB occurrence.

The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS - 22.0, IBM, Armonk, NY, USA), with the significance level set to 5% ($P < 0.05$). The Kolmogorov Smirnov test was used for verifying the distribution of the sample. The Student T-test and Chi-square were used to compare age and gender between the groups. The bivariate analysis was applied considering 95% confidence intervals (95% CI). The variables with a P value ≤ 0.2 were incorporated into the multiple logistic regression analysis; and those variables subsequently achieving a P value < 0.05 were considered significant and remained in the final model [38].

Results

A total of 74 dental inflammations were found in both groups. The most common type was dental inflammation of endodontic origin (34 individuals or 45.95%).

Eighty eight percent of the control group presented dental inflammation. Seventy individuals of the control group had no dental inflammation (92.1%) (Table 1).

Dental inflammation of endodontic origin (Figure 2A) and of combined endodontic and periodontal origin (Figure 2B) were the most commonly type found (20 cases each one) among the exams with MCB.

Vertical or horizontal bone lost were also found among the CBCTs of the case group, in a minor prevalence (Figure 2C). Pericoronitis was found only in the control group (Figure 2D).

Thirty nine exams of the case group presented higher gray levels.

The initial bivariate analysis found statistically significant association between MCB and dental inflammation, as well as between MCB and gray level values ($P < 0.001$).

A multiple logistic regression analysis was performed to further support the statistical analysis in order to verify whether one of the independent variables would be more relevant for MCB occurrence. The results indicated that the dental inflammations offer a major risk for the occurrence of MCB ($P<0.001$). The patients with dental inflammations had 11.640 times more chances of presenting branches compared to those without dental inflammation ($P<0.001$; CI 95%: 4.327-31.311).

The higher levels of gray values increased the chances of showing branches by 1.002 ($P = 0.002$; CI 95%: 1.001-1.003). It means that the higher gray levels played a minor role in the MCB occurrence ($P = 0.002$) (Table 2).

Discussion

To improve the knowledge about the effects of inflammation over mandibular innervation, the present epidemiological study organized the case and control groups considering the MCB arising around the posterior teeth as the dependent variable.

It must be emphasized that the refined CBCT evaluation of the mandibular canals improved the MCB assessment [24-30,35,39], and enabled us to detect intricate branches not yet described and without adequate classification in the literature. Despite some branches seem similar to the ones previously described by Naitoh et al. [28] or Kieser et al. [40], it was not possible to recognize them as the same. The Naitoh et al.'s [28] classification refers to branches started in the ramus region, which is a different location from the branches evaluated in the present study, originated in the posterior region of the alveolar ridge. Likewise, the findings of Kieser et al. [40] were on edentulous mandibles (cadaver), lacking adequate information about their locations in relation to teeth. In addition, the branches found in the dissections were not detected by the researchers in their radiographic evaluation.

The typical aspect of the branches toward dental inflammations, along the association found between MCB and dental inflammation, led us to hypothesize that the dental inflammation and MCB are somehow related. Our suspicion refers to an action of inflammatory endogenous agents derived from the inflammatory process over the inferior alveolar neurovascular bundle. Supporting this suspicion, prior immunohistochemical studies have already detected that the tissues involved in angiogenesis, bone remodeling and neurogenesis present specific receptors for endogenous factors released by inflammation [41-45]. Although it is a novelty, the hypothesis of a postnatal remodeling of the mandibular canals supports previous reports of mandibular canals alterations derived from uncongenital pathologic conditions [11,12].

An important issue that could raise doubts about the clinical relevance of these findings would be related to the presented MCB contain only blood vessels as a result of a common phenomenon derived from inflammatory responses (angiogenesis) [9,46]. However, the imaging assessment of MCB assumes the presence of inferior alveolar nerve branches within the branches due to their origin from the main mandibular canal [24]. Besides, the presence of the inferior alveolar neurovascular branch within the MCB was scientifically already detected by means of histological assessment [21,47].

Even the MCB was just restricted to a vascular alteration, it would be still important to inform clinicians about this morphological alteration, in order to avoid bleeding during surgical procedures that can be significant according to the branches caliber.

Although the initial bivariate analysis had suggested that the bone marrow gray level had also presented an association with MCB, the multiple logistic regression analysis showed that it only played a minor role. This variable was assessed because it was thought that its increases could contribute to detection of pre-existing canals by improving the contrast between hard and soft tissues (bone marrow and canals) [48]. However, this result can be considered normal, since inflammation can increases the bone density, just as a physiologic response like osteitis, and suggesting that the gray level has acted as a confounding variable.

Regarding the dental inflammations found, those of endodontic origin and of combined endodontic and periodontal origin were most frequent. This is in accordance with the findings by Awad [49] who reported dental inflammation of the endodontic origin as the most common pathological alterations affecting the maxillary and mandibular alveolar ridges, with greater proportions in the posterior regions of the mandibles. This finding is also related with our previous considerations regarding endogenous interactions between mediators delivered by dental inflammation and the tissues. Some previous studies have already detected an interaction between inflammatory mediators and intraosseous pathological growth, osseous remodeling, angiogenesis, and neurogenesis [50-52].

It is important to highlight that the diagnosis of the mandibular canals and their branches has an important clinical significance. Surgical accidents can cause harmful and permanent post-operative sensory disturbances to patients derived from several dental procedures such as extractions of non-erupted teeth, orthognathic surgery, implant insertions, endodontic procedures, as well other surgical procedures [13-20]. According to the American Academy of Oral and Maxillofacial Radiology [53], adequate surgical planning based on CBCT scans along with the knowledge of anatomy and physiology can contribute to reduced undesirable surgical complications.

Since our study detected an association between the analyzed variables, it is important to inform clinicians about this finding. It can be useful for predicting the location of MCB, avoiding harmful complications derived from surgical and anesthetics procedures, and opening up the possibility of observing the situation, evaluating it and collecting more evidences. The possibility of a post natal neurovascular remodeling is scientifically very exciting and opens new perspectives for the treatment of patients with neurovascular injury.

Future research should further study this assessment in order to verify if there is, in fact, a causal relationship between dental inflammation and MCB through a longitudinal set-up.

Conclusions

There is an association between MCB situated around the posterior mandibular teeth and dental inflammation. The dental inflammations of endodontic origin are most often associated with the branches.

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Tables

Table 1 - Distribution of dental inflammations

	Group		
	Case (%)	**Control (%)**	**Total**
Endodontic	20 (58.8%)	14 (41.2%)	34 (100%)
Combined endodontic and periodontal	20 (71.4%)	08 (28.6%)	28 (100%)
None	06 (07.9%)	70 (92.1%)	76 (100%)
Periodontal	04 (40.0%)	06 (60.0%)	10 (100%)
Pericoronitis	00 (00.0%)	02 (100%)	02 (100%)
Total	50 (33.3%)	100 (66.7%)	150 (100.0%)

Table 2 - Distribution and association of dental inflammation, gray level and mandibular canal branching

	Groups		Adjusted OR (CI 95%)	*P*
	Case (%)	**Control** (%)		
Dental inflammation				
Yes	44 (88.0%)	30 (30.0%)	11.640 (4.327-31.311)	<0.001
No	06 (12.0%)	70 (70.0%)		
Gray level				
> 543.793	39 (78%)	29 (29%)	1.002 (1.001-1.003)	0.002
up to 543.793	11 (22%)	71 (71%)		

Figures

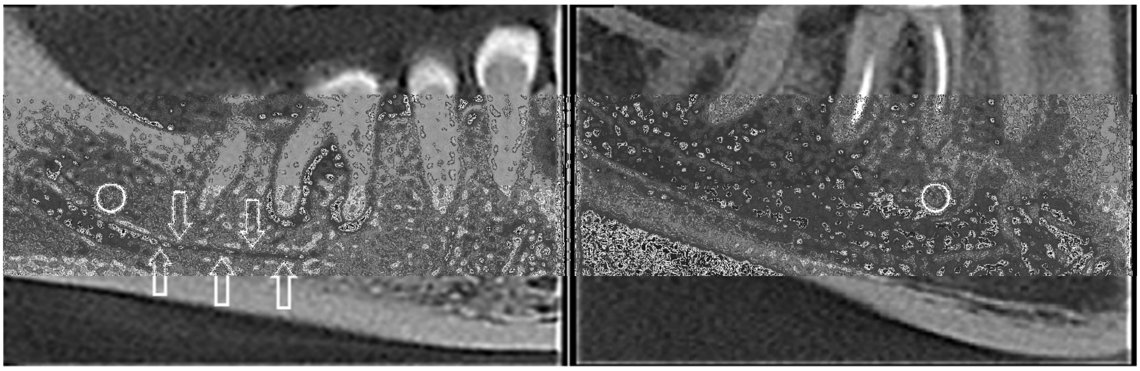

Figure 1. A - Gray level measurement in the case group, with standardized area (white circle), just above the region of the mandibular canal branching origin. White arrows showing the mandibular canal branching; **B**- Gray level measurement in the control group, with standardized area (white circle), just above the mandibular canal and below to mesial root of the first molar.

Figure 2. A – White arrows: multiple mandibular canal braching toward dental inflammation of endodontic origin on mesial and distal roots, and horizontel bone lost between the roots as well; **B** - White arrows showing double mandibular canal braching anteriorly and posteriorly toward a combined endodontic and periodontal dental inflammation; **C**– Orthorradial slice showing a mandibular canal braching (white arrow) toward a lingual vertical bone loss; **D** – Pericoronitis affecting a third molar in an exam without mandibular canal branching (control group).

7 – Considerações Finais

Foi observada alta prevalência de ramificações dos canais mandibulares (41,1%), com localizações e morfologias variadas, sem associação com os gêneros dos pacientes.

Ramificações dos canais mandibulares detectadas nos ramos mandibulares encontraram descrição e classificação na literatura.

Ramificações detectadas nos corpos mandibulares apresentaram considerável diversidade morfológica, sem adequada descrição ou classificação prévia na literatura.

De acordo com a caracterização elaborada para as ramificações encontradas nos corpos mandibulares, o tipo mais comum foi ramificação simples, direcionada para superior e em contato com lesões inflamatórias na região do terço apical.

A ocorrência simultânea de ramificações e lesões dentárias inflamatórias nos corpos mandibulares foi observada com frequência, com associação estatisticamente significativa, e constitui achado inédito na literatura.

Considerando estudos que demonstraram a neuroplasticidade e capacidade de reparação neuronal, a associação detectada diverge da teoria embrionária sobre a origem das ramificações dos canais mandibulares e contempla a possibilidade do desenvolvimento pós-natal das ramificações.

As lesões inflamatórias mais comumente detectadas nas avaliações foram lesões apicais com origem endodôntica e lesões endoperio. O envolvimento endodôntico em ambas as lesões mais prevalentes sugere a possível ação de fator predisponente específico endodôntico.

Os níveis de cinza apresentaram associação mais fraca com a ocorrência das ramificações dos canais mandibulares. Infere-se que representem variável de confundimento, tendo em vista que o aumento da densidade óssea pode ser uma consequência da presença de lesões inflamatórias.

O conjunto de achados permite inferir maior previsibilidade quanto à ocorrência de ramificações dos canais mandibulares, reduzindo o risco de acidentes com lesões neurovasculares durante procedimentos cirúrgicos.

Em futuros estudos, a identificação de um possível fator endógeno de estimulação da neurogênese e angiogênese em estruturas do complexo dentomaxilofacial pode abrir boa perspectiva para o desenvolvimento de terapias para a reparação de lesões neurovasculares.

8 - Conclusões

Foi observada alta prevalência de ramificações dos canais mandibulares nos corpos mandibulares com lesões inflamatórias.

A presença de lesões inflamatórias aumentou as chances para a ocorrência de ramificações dos canais mandibulares.

As lesões mais comumente associadas com as ramificações dos canais mandibulares foram de origem endodôntica.

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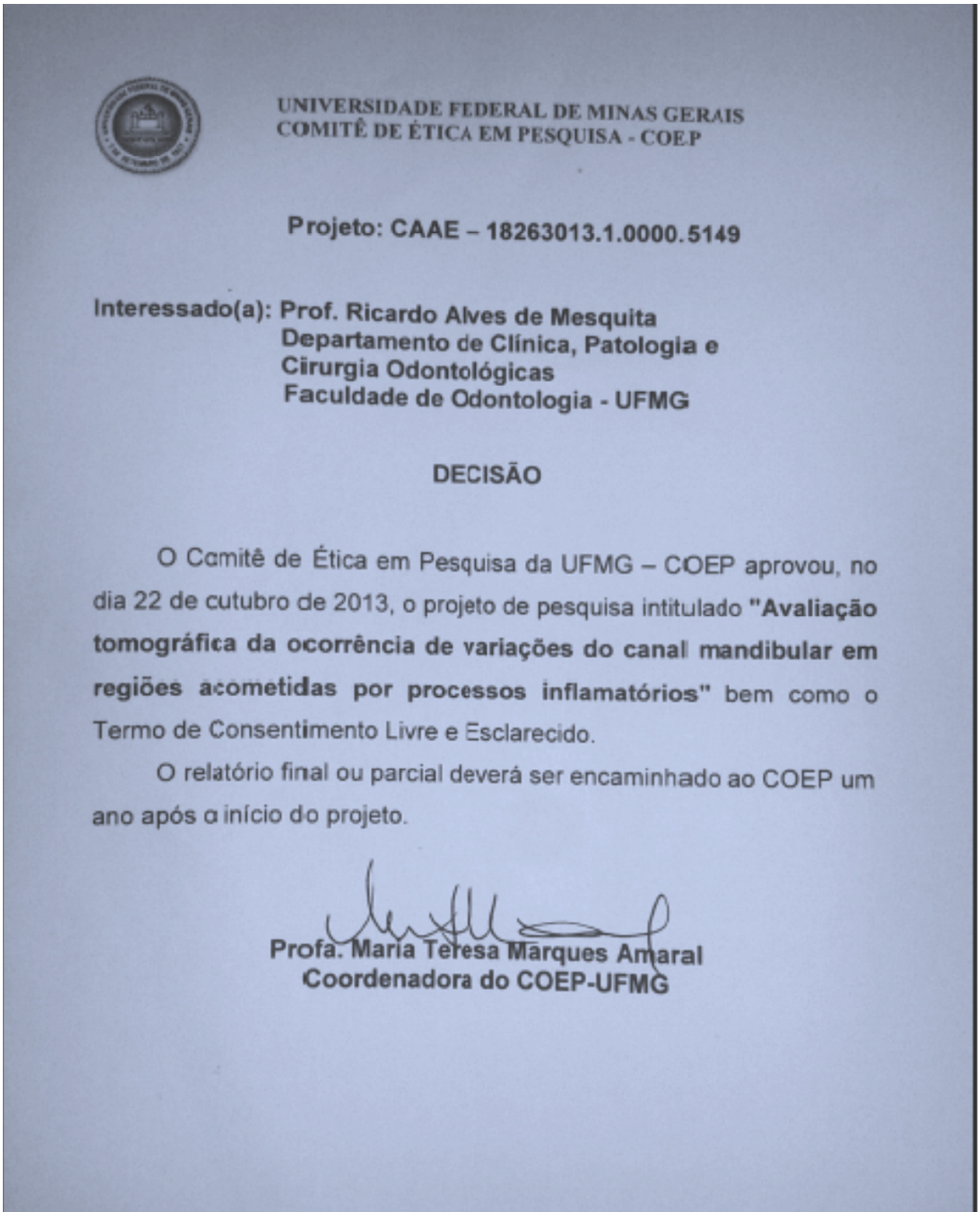
ANEXOS

Anexo 1 – Aprovação COEP



UNIVERSIDADE FEDERAL DE MINAS GERAIS
COMITÊ DE ÉTICA EM PESQUISA - COEP

Projeto: CAAE – 18263013.1.0000.5149

Interessado(a): Prof. Ricardo Alves de Mesquita
Departamento de Clínica, Patologia e Cirurgia Odontológicas
Faculdade de Odontologia - UFMG

DECISÃO

O Comitê de Ética em Pesquisa da UFMG – COEP aprovou, no dia 22 de cutubro de 2013, o projeto de pesquisa intitulado **"Avaliação tomográfica da ocorrência de variações do canal mandibular em regiões acometidas por processos inflamatórios"** bem como o Termo de Consentimento Livre e Esclarecido.

O relatório final ou parcial deverá ser encaminhado ao COEP um ano após o início do projeto.

Profa. Maria Teresa Marques Amaral
Coordenadora do COEP-UFMG

Av. Pres. Antonio Carlos, 6627 – Unidade Administrativa II - 2º andar – Sala 2005 – Cep:31270-901 – BH-MG
Telefax: (031) 3409-4592 - e-mail: coep@prpq.ufmg.br

Anexo 2 – Termo de Consentimento Livre e Esclarecido

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

A pesquisa “AVALIAÇÃO TOMOGRÁFICA DA OCORRÊNCIA DE VARIAÇÕES DO CANAL MANDIBULAR EM REGIÕES ACOMETIDAS POR PROCESSOS INFLAMATÓRIOS” é um projeto de pesquisa para elaboração de tese de Doutorado em Estomatologia, na Faculdade de Odontologia da Universidade Federal de Minas Gerais (UFMG). Seus objetivos são melhorar a compreensão das inervações das mandíbulas, para otimizar o planejamento de intervenções nessas regiões e desvendar se uma lesão inflamatória pode estimular a proliferação de vasos sanguíneos e nervos. Para isso, é necessária a avaliação de mandíbulas em exames de tomografias computadorizadas.

Para que possamos avaliar as imagens do seu exame, você terá que dar sua permissão.

Como o exame foi solicitado pelo seu dentista, não será necessário realizar nenhum outro exame e nenhum custo adicional lhe será cobrado.

Caso você autorize, sua privacidade será respeitada, não havendo nenhuma possibilidade de você ser identificado. Ainda lhe será garantido o direito de retirar sua autorização, em qualquer momento, se assim desejar.

Caso você não queira participar, você será atendido normalmente.

Esta pesquisa foi aprovada pela Comitê de Ética em Pesquisa da UFMG.

AUTORIZAÇÃO

Sendo assim, eu, ____, me declaro devidamente informado(a) sobre os propósitos da pesquisa e concordo, por minha livre escolha, permitir a avaliação das imagens de meu exame.

Belo Horizonte, _______ de ____________________ de 20__.

____

Nome e nº Carteira Identidade

Qualquer dúvida poderá ser esclarecida pelos pesquisadores:

PROF. MAURÍCIO AUGUSTO AQUINO DE CASTRO (Fone: 31-8214-0904)

PROF. DR. RICARDO ALVES MESQUITA