PONTIFÍCIA UNIVERSIDADE CATÓLICA DO PARANÁ

ESCOLA DE CIÊNCIAS DA VIDA
PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA
ÁREA DE CONCENTRAÇÃO ESTOMATOLOGIA

ANDRÉ TSCHOEKE

FIBROMA ODONTOGÊNICO PERIFÉRICO: UMA REVISÃO SISTEMÁTICA

Curitiba
2017

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Dissertação apresentada ao Programa de Pós-Graduação em Odontologia da Pontifícia Universidade Católica do Paraná, como parte dos requisitos para obtenção do título de Mestre em Odontologia, Área de Concentração em Estomatologia.

Orientadora: Profa. Dra. Aline Cristina Batista Rodrigues Johann.

Curitiba
2017

Agradecimentos

À Deus por me permitir chegar até onde cheguei, e sempre me mostrar o melhor caminho para as decisões.

A Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) por contribuir com meus ensinos disponibilizando bolsa integral para o mestrado.

À Pontifícia Universidade Católica do Paraná e ao Programa de Pós-graduação em Odontologia por confiar em mim e ceder seus espaços para poder realizar meu aprendizado e aos seus funcionários, que sempre estiveram disponíveis para me ajudar.

À professora Aline Cristina Batista Rodrigues Johann por me mostrar pela primeira vez o mundo da pesquisa científica ainda na época da graduação e por confiar em mim para passar todos seus conhecimentos sobre Odontologia.

Aos professores Sérgio Vieira e Renata Iani Werneck pela coordenação e aos demais professores do Programa de Pós-Graduação em Odontologia por me ensinarem os mais diversos conhecimentos na Odontologia.
Aos professores Paulo Henrique Couto Souza e Rodrigo Nunes Rached pelas relevantes e fundamentais considerações na qualificação deste trabalho.

À minha família, namorada, amigos por aceitarem minha ausência para que eu pudesse me dedicar com todas as forças a este trabalho.

Aos colegas e agora novos amigos do mestrado e doutorado pelo companheirismo, parceria e ensinamentos durante esta jornada.

A todos que, de forma direta ou indireta sempre estiveram torcendo pelo meu sucesso neste período do mestrado.

“A tarefa não é tanto ver aquilo que ninguém viu, mas pensar o que ninguém ainda pensou sobre aquilo que todo mundo vê. ”

Arthur Schopenhauer

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Autores:

1. André Tschoeke, DDS
2. Aline Cristina Batista Johann, DDS, MSc, PhD

AFILIAÇÃO INSTITUCIONAL:

Pontifícia Universidade Católica do Paraná, School of Life Sciences, Rua Imaculada Conceição, 1155, Prado Velho 80.215-901, Curitiba, PR, Brazil.

Autor correspondente

Profa. Aline Cristina Batista Rodrigues Johann. PhD

Clínica de Odontologia-Pontifícia Universidade Católica do Paraná

Rua Imaculada Conceição, 1155, Prado Velho 80.215-901 Curitiba, PR, Brazil.

Telephone number: +55 41 3271-2592 Fax number: +55 41 3271-1405

E-mail: alinecristinabatista@yahoo.com.br

Contagem de palavras: 2354

Nº resumo:346

Nº figuras: 1

Nº tabelas:5

Nº ref.:69

Principal descoberta: A partir da revisão sistemática, verificou-se que a literatura sobre o fibroma odontogênico periférico é carente de trabalhos com maior nível de evidência científica, como uma revisão sistemática, além de necessitar de um maior rigor científico na qualidade dos relatos e séries de caso.

Resumo

Introdução: O fibroma odontogênico periférico (FOP) é uma neoplasia odontogênica mesenquimal benigna caracterizada como uma massa gengival firme, geralmente séssil e de cor semelhante à mucosa normal. Estudos têm descrito essa lesão de forma isolada, sem o agrupamento das informações o que se fez necessário a elaboração de uma revisão sistemática para identificar as características predominantes nesta lesão, sendo este o objetivo do presente estudo. **Métodos**: Foram incluídos artigos em inglês, com humanos, com diagnóstico histológico de FOP, contendo pelo menos uma de cada das características epidemiológicas, clínicas e histológicas. A busca de artigos, e extração de dados foram conduzidos independentemente e em duplicata e a busca de publicações com palavras-chave, nas bases de dados Pubmed, BVS, Cochrane, Science Direct e Scopus, incluindo artigos inseridos até novembro de 2016. **Resultados:** De um total de 964 artigos, foram excluídos 908 após aplicação dos critérios de elegibilidade, sendo elegíveis 49, sendo 28 artigos de relato de caso e 21 artigos de estudos de caso. Desses artigos, totalizaram 539 casos clínicos de pacientes com FOP. As características epidemiológicas mais frequentes foram mulheres, da etnia branca, entre 2ª e 4ª década de vida. A lesão apresentou-se, com tempo de evolução médio de 3,04 anos. Clinicamente, predomina em gengiva mandibular posterior ou anterior, como nódulo, ulcerado ou não e séssil. Os principais achados histopatológicos foram ausência de ulceração do epitélio superficial, tecido conjuntivo fibrocelular, podendo ou não apresentar calcificações, com a presença abundante ou escassa de ilhas e cordões de epitélio odontogênico. Em alguns artigos verificou-se a ausência de informações, falta de imagens, imagens de difícil visualização, legendas com informações ausentes, informações que necessitaram ser coletadas por meio da imagem e agrupamento de dados. **Conclusão:** A literatura exibe artigos descrevendo as características da lesão, em grande parte de forma incompleta, carecendo de trabalhos com maior nível de evidência científica, como uma revisão sistemática, além de necessitar de um maior rigor científico na qualidade desses artigos. Mesmo com as limitações, ainda foi possível identificar as características predominantes do FOP e que a presença de epitélio odontogênico para defini-lo histologicamente precisa ser avaliado.

Palavras-chave: Odontogenic Tumor, Fibroma, Human

Introdução

Fibroma odontogênico é descrito pela Organização Mundial de Sáude (OMS) em 2017, “como um raro neoplasma do tecido conjuntivo fibroso maduro com quantidade variável de epitélio odontogênico de aparência inativa com ou sem evidência de calcificação”. Esta lesão pode ser encontrada tanto no interior dos ossos da mandíbula ou podem ser encontrados na mucosa bucal. [1]O Fibroma Odontogênico Periférico (FOP) é considerado o equivalente extra ósseo do Fibroma Odontogênico Central. [1-2] O primeiro artigo que relata um caso de fibroma odontogênico periférico data de 1958,[3] e a partir de então, estudos foram conduzidos, mas nenhuma revisão sistemática foi realizada.

Clinicamente, o FOP se apresenta como massa gengival firme, geralmente séssil, com crescimento lento, indolor, e de cor semelhante a mucosa adjacente.[2,4,5] Radiograficamente, o FOP pode apresentar ocasionalmente áreas de radiopacidade, porém não afeta o osso adjacente.[2] Os diagnósticos diferenciais clínicos do FOP são a hiperplasia fibrosa inflamatória, fibroma, fibroma ossificante periférico, granuloma de células gigantes periféricos e granuloma piogênico.[7] O tratamento é excisão local da lesão, e o prognóstico é excelente, com raras recorrências.[4,5]

Estudos e relatos de casos têm descrito essa lesão de forma isolada, sem o agrupamento das informações.[8] É de suma importância documentar essa lesão, pois pode revelar variações em suas características, além de auxiliar no estabelecimento do correto diagnóstico, histopatologia, opção de tratamento e taxa de recorrência (Reddy et al. 2014). Muito além de documentar, é imprescindível agrupar com método estas informações, de forma que se faz necessária a elaboração de uma revisão sistemática para determinar as características epidemiológicas, clínicas e histológicas predominantes nesta lesão, pois publicações revisadas ressaltam lacunas nas áreas de diagnóstico,[9] sendo essa a justificativa do presente estudo, o que poderá auxiliar a conduta do cirurgião-dentista em casos semelhantes. Revisões sistemáticas ajudam os profissionais a se atualizarem, resumindo grandes estudos e discutindo a diferença do ponto de vista deles sobre um mesmo tema abordado[6]. Revisões sistemáticas de características clinicas e radiográficas de lesões bucais e dos maxilares tem sido conduzidas em: hiperplasia fibrosa inflamatória,[9] melanoacantoma,[10] linfoma,[11] cisto odontogênico ortoqueratinizado,[12] tumor ceratocisto odontogênico[13] e cisto glandular odontogênico.[14]

O objetivo do estudo foi identificar as características epidemiológicas, clínicas e histológicas do FOP , por meio de uma revisão sistemática.

Metodologia

Revisão sistemática

O protocolo de revisão sistemática se baseou nos critérios apresentados pelo do *Preferred Reporting Items for Systematic Reviews and Meta-Analyses*, o PRISMA.[25]

Questão de pesquisa clinicamente relevante: Qual é o perfil epidemiológico, clínico e histológico do FOP?

Critérios de Inclusão: Artigos em língua inglesa, com indivíduos (humanos) com diagnóstico histológico de FOP e contemplando pelo menos uma de cada das características epidemiológicas, clínicas ou histológicas.

Critérios de Exclusão: Revisões de literatura e artigos não definiam tipo de lesão (central ou periférica/ fibroma odontogênico ou fibroma ossificante).

Fontes de dados: Foi realizada a busca de artigos National Library of Medicine (NLM- interface PubMed), e a Biblioteca Virtual em Saúde (BVS), Cochrane, Science Direct e Scopus, incluídos nas plataformas até o mês de novembro de 2016.

Expressões de Busca no PubMed (Anexo F): (((Peripheral odontogenic fibroma) OR ((("Odontogenic Tumors"[Mesh]) AND "Fibroma"[Mesh])) AND ((("Diagnosis"[Mesh]) OR odontogenic epithelium[Title/Abstract]) OR (nets[Title/Abstract] OR islands[Title/Abstract]) OR histopathology)) AND ((((((((("Gender Identity"[Mesh]) OR "Sex"[Mesh]) OR male[Title/Abstract]) OR female[Title/Abstract]) OR man[Title/Abstract]) OR woman[Title/Abstract])) OR (((((("Age of Onset"[Mesh]) OR years[Title/Abstract]) OR Onset Age[Title/Abstract]) OR Age-at-Onset[Title/Abstract]) OR Age at Onset[Title/Abstract])) OR (((((((("Disease Attributes"[Mesh]) OR clinical characteristics[Title/Abstract]) OR Attribute, Disease[Title/Abstract]) OR Attributes, Disease[Title/Abstract]) OR Disease Attribute[Title/Abstract]) OR nodule[Title/Abstract]) OR sessile[Title/Abstract]) OR pedicellate[Title/Abstract]) OR gingival mass[Title/Abstract]))) OR "Humans"[Mesh])))

A busca de artigos, e extração de dados foram conduzidos independentemente e em duplicata, sendo as divergências sobre os casos solucionadas por um terceiro avaliador. Inicialmente, retirou-se os artigos em duplicata, seguido pela eliminação dos artigos que não se enquadraram nos critérios de elegibilidade. Tabulou-se os artigos em Excel, procedendo o processo de extração de dados, sendo inclusos informações referentes aos artigos: a) autoria, ano de publicação, número de casos; b) aspectos epidemiológicos: etnia e gênero dos participantes, idade; c) anamnese: sinais e sintomas, tempo de evolução; d) aspectos clínicos: localização lesão fundamental, ulceração, inserção, cor, superfície, tamanho, deslocamento dentário; e) aspectos histopatológicos: Ilhas ou cordões de epitélio odontogênico, quantidade, epitélio semelhante a ameloblastoma, epitélio com diferencial para células claras, tipo de tecido conjuntivo, ulceração do epitélio de superfície, células basais em brotos, presença de calcificação, lesão encapsulada; f) recorrência.

Para inserir a década a qual os pacientes pertenciam, foi feita a média da idade e convertida em décadas. Para a evolução da lesão foi obtido a média de anos dos casos por artigo e para cálculo do tamanho foi realizada média em cm por artigo.

Resultados

Foram encontrados um total de 964 artigos, sendo que 895 foram excluídos por não serem artigos sobre FOP e 1 artigo por fazer estudo imunohistoquímico comparativo com outras lesões e não revelando as características epidemiológicas, clínicas e histopatologicas. Outros 15 foram excluídos por serem artigos apenas encontrados em outras línguas que não o inglês e 11 por não serem encontrados, mesmo após solicitação aos autores, comutação bibliográfica e tentativa de compra, totalizando 907 artigos excluídos nesta fase de triagem. Os textos completos de 58 artigos potencialmente elegíveis foram lidos, e 9 foram excluídos por se tratarem ou de uma revisão de literatura, ou de fibroma periférico (sem determinar se era odontogênico ou ossificante), ou de fibroma ossificante periférico, ou por não apresentar pelo menos uma de cada característica epidemiológica, clínica e histológica da lesão. O anexo A mostra os artigos eliminados nesta fase com suas respectivas justificativas. Um total de 49 estudos preencheram critérios de inclusão,

desses 28 artigos eram relatos de casos e 21 artigos com séries de casos. O fluxograma 1 ilustra esse processo de seleção dos artigos.

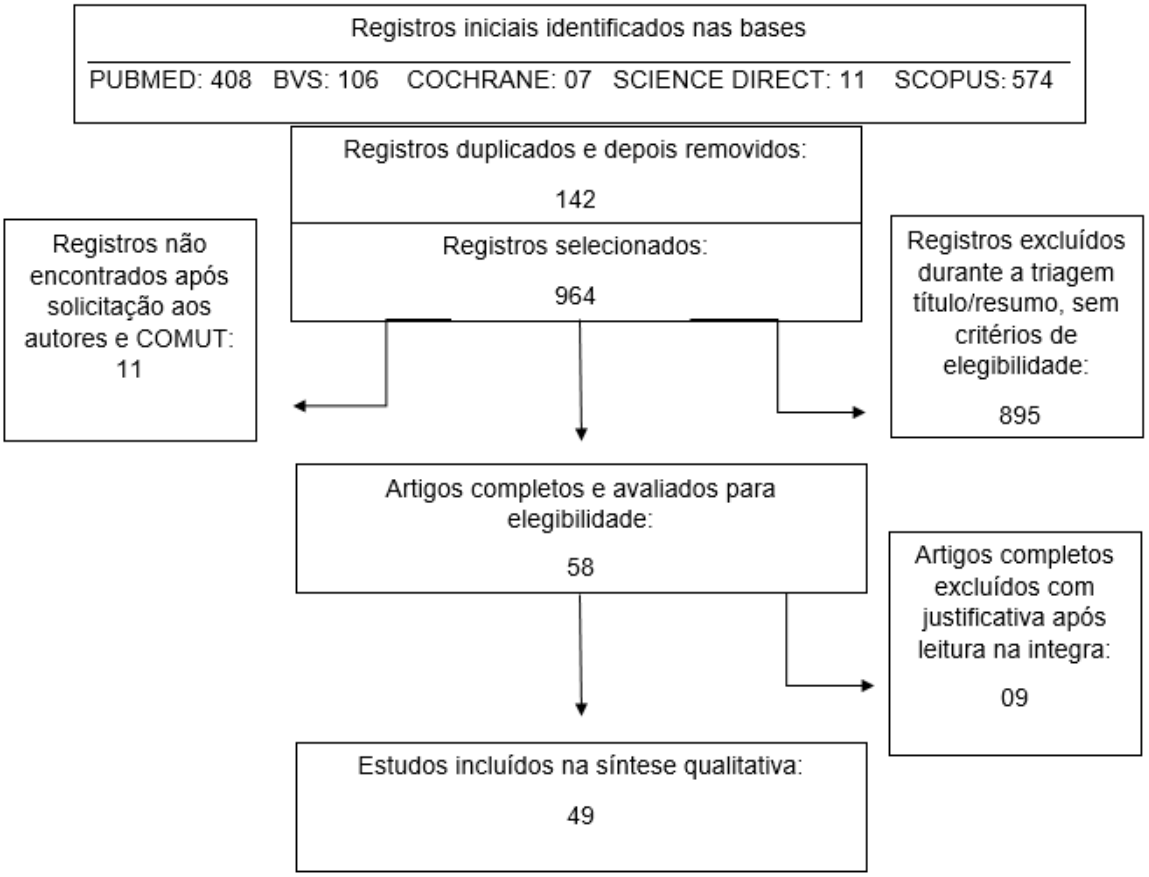

Figura 1: Fluxograma para a seleção dos artigos.

Dos 49 artigos foram identificados 539 casos de pacientes portadores de FOP. Autorias, número de casos por artigo, características epidemiológicas, sinais e sintomas e tempo de evolução mais frequentes do FOP estão dispostas na tabela 1. Nas tabelas estão dispostos os resultados quanto as características clínicas (tabela 2) e histológicas (tabelas 3 e 4) encontradas na revisão sistemática. No anexo C, as características clínicas e histológicas estão distribuídas de acordo com o artigo dos quais elas foram extraídas. Em todos os casos, a excisão cirúrgica foi a opção de tratamento e a taxa de recorrência da lesão foi de 10,58% dos casos, enquanto 66,41% dos casos não apresentaram recorrência. Em 23,01% dos casos, essa informação não foi citada.

Tabela 1. Autoria, ano de publicação, número de casos, idade, sexo, etnia dos indivíduos, sinais e sintomas e tempo de evolução em casos de fibroma odontogênico periférico.

Referências	Ano	nº casos	Idade (Década)	Sexo	Etnia	Sinais e sintomas	Evolução (anos)
Buckman[3]	1958	1	6ª	F	A	*	14
Farman[15]	1975	10	Média3ª	6M/4F	9N/1B	10*	*
Lownie et al.[4]	1976	1	4ª	F	N	Não	0,16
McGuff et al. [16]	1981	1	2ª	M	B	Não	0,33
Klein[17]	1982	1	3ª	M	B	*	0,16
Harisson et al.[18]	1983	1	2ª	F	*	*	3
Pockrass et al.[19]	1983	1	7ª	F	B	*	*
Mulcahy & Dahl[20]	1985	52	Média4ª	13M/39F	47B/5*	52*	Média3,75
McGnnis & Ray[21]	1985	1	3ª	F	B	Não	2
Buchner et al.[5]	1987	9	Média5ª	5M/4F	6B/2N/1A	Sangue: 1/ 8*	Média0,55
Buchner[22]	1989	5	Média4ª	2M/3F	5*	5*	Média0,775
Kenney et al[23]	1989	13	Média2ª	8M/5F	8B/4N/1*	13*	*
Slabbert & Altini[24]	1991	30	Média3ª	16M/12F/2*	28N/2*	30*	*
Michaelides[7]	1992	1	6ª	F	B	Não	0,08
Weber et al[25]	1992	3	Média3ª	1M/2F	2N/1B	3*	Média3
Ficarra et al[8]	1993	1	2ª	F	B	*	*
Daley & Wysocki[27]	1994	36	Média4ª	12M/24F	14B/1N/21*	Não: 7/ 29 *	Média2,24
Siar& Ng[28]	1995	2	Média4ª	1M/1F	2A	2*	Média1
Siar& Ng[29]	1995	1	7ª	F	A	*	0,33
Siar& Ng[30]	2000	46	Média4ª	20M/26F	46*	Dor, sangramento: 16 / 30*	Média2
Flaitz[31]	2001	1	2ª	M	N	Não	*
Manor et al[32]	2004	2	4ª	*	2*	2*	*
Martelli-Júnior et al[33]	2006	1	1ª	F	B	*	0,33
Buchner et al.[34]	2006	23	Média4ª	11M/12F	19B/2N/1A	23*	*
Bonetti et al[35]	2006	1	2ª	M	B	*	3
Bosco et al[36]	2006	1	2ª	F	B	Desconforto	0,5
Garcia et al.[37]	2007	17	4ª	2M/15F	11B/2N/4*	Não: 4/13*	*
Rinaggio et al[38]	2007	1	6ª	F	*	Não	0,16
Lin et al[39]	2008	25	Média4ª	9M/16F	25A	25*	*
Ide et al[40]	2008	1	2ª	1F	A	*	3
Alaeddini et al[41]	2010	19	Média 4ª	11M/8F	19*	19*	*
Ritwik & Brannon [42]	2010	151	Média4ª	65M/86F	97B/46N/8*	151*	Média20
Ramachandra et al[43]	2011	1	2ª	M	*	*	10
Baiju & Rohatgi[59]	2011	1	3ª	F	*	*	1
Brooks&Nikitakis[44]	2011	1	3ª	F	B	Sangramento	6
Patel et al[45]	2011	1	4ª	M	B	Não	*
Eversole [46]	2011	40	4ª	13M/27F	40*	40*	*
Lin et al[47]	2011	12	4ª	6M/6F	12*	12Não	Média1,5
Silva et al[48]	2012	1	2ª	F	B	Não	1
Wood et al[49]	2012	1	7ª	F	*	*	*
Livada et al[50]	2013	1	3ª	M	N	Não	2
Wu et al [51]	2013	10	Média4ª	7M/3F	10*	10*	*
Soileau[52]	2013	1	6ª	F	N	*	10
Reddy et al [53]	2014	1	5ª	F	N	*	1
Sreeja et al[54]	2014	1	6ª	M	N	Não	0,5
Kumar et al[55]	2014	1	3ª	F	*	*	5
Truschnegg et al[56]	2015	3	Média3ª	3F	3*	3*	*
Silva et al[57]	2016	3	Média3ª	2M/1F	1B/1N/1P	3Não	Média1,47
Bharathi et al. [58]	2016	1	6ª	M	*	Não	0,5
Total (%)		539	1ª: 2,05 2ª:20,40 3ª:22,45 4ª:32,65 5ª:4,08 6ª:12,25 7ª:6,12	4(0,75)* 219(40,63) M 316(58,62) F	218(40,45) B 107(19,85) N 32(5,94) A 1(0,18) P 181(33,58) *	19(3,52)Sintoma 26(4,83) Não 494(91,65) *	Média:3,04 anos

Legenda: M= masculino, F= feminino, A= amarelo, B= branco, N= negro, P= pardo , *= não relatado

Tabela 2. Localização, maxilar envolvido, região, lesão fundamental, presença de ulceração, inserção, cor, superfície, tamanho, deslocamento dentário em casos de fibroma odontogênico periférico.

Variáveis/ total (%)	Localização	Maxila ou mandíbula	Região	Lesão	Ulcerado	Inserção	Cor	Superfície	Tamanho (cm)	Deslocamento dentário
	8 (1,49) RA	257(47,69) Md	92(17,06) Posterior				5(0,93)R	20(3,72)Li		14(2,60) Sim
	495 (91,84)G	190(35,25) Mx	82(15,40)	213(39,52)N	74(13,73)Sim	192(35,62)S	112(20,77)V	12(2,22)Lo	Média	65(12,05)Não
	36 (6,67)*	92(17,06) *	Anterior	111(20,60)A	86(15,95)Não	93(17,25)P	42(7,80)SM	507(94,06)	tamanho=	460(85,35)*
			364(67,54)*	196(39,88)*	379(70,32)*	254(47,13) *	380(70,50)*	*	1,71	

Legendas: RA= Rebordo alveolar, G=Gengiva, Md= Mandíbula, Mx= Maxila, A= Aumento de volume, N= Nódulo, S= Séssil, P= Pediculado, R= Rosa, V= vermelho, SM= semelhante a mucosa, Lo= Lobulada, Li= Lisa, *=Não Informado

Tabela 3: Grau de ulceração do epitélio de superfície, tipo de tecido conjuntivo, presença de calcificações/osso/dentina, presença de cápsula em fibromas odontogênicos periféricos.

Nº Casos	Grau de ulceração do epitélio de superfície	Tipo de Tecido Conjuntivo	Calcificação	Osso	Cementóide	Dentina	Calcificação distrófica	Cápsula
	132(24,48) NU	220(40,82) FC/						2(0,37) Sim
	/28(5,20)MOD/	146(27,08) MX/	234(43,41)Não					
Total	12(2,23) EU/	14(2,60) FH/	248(46,01)Sim	116(21,52)Sim	118(21,89) Sim	28(5,20) Sim	42(7,80) Sim	102(18,92) Não
(%)	367(68,09)*	159(29,50)*	57(10,58)*	423(78,48)*	421(78,11)*	511(94,80)*	496(92,20)*	435(80,71)*

Legenda: NU= não ulcerado Mod= moderado, EU= extensivamente ulcerado, FC= Fibrocelular, MX= mixóide, FH= fibrohialinizado, *= Não informado

Tabela 4: Ilhas e cordões de epitélio odontogênico, quantidade, epitélio semelhante a ameloblastoma, epitélio com diferencial para células claras, e presença de células basais em brotos nos fibromas odontogênicos periféricos.

Nº casos	Ilhas ou cordões de epitélio odontogênico	Quantidade	Epitélio semelhante a ameloblastoma	Epitélio com diferencial para células claras	Células basais em brotos
		74(13,73) Abundante			
	463(85,90) Sim	39(7,24) Moderado			
	48(8,90) Não	74(13,73)Escasso	5(0,93) Sim	3(0,55) Sim	39(7,23) Sim
Total (%)	28(5,20)*	352(65,30)*	534(99,07)*	535(99,45)*	500(92,77)*

*= Não informado

A tabela 5 apresenta as principais dificuldades encontradas no momento da extração e análise de dados e no anexo D, as principais dificuldades estão dispostas de acordo com seu artigo de origem.

Tabela 5- Dificuldades encontradas em cada artigo

Ref.	Dados clínicos Incompletos	Dados histopatológicos incompletos	Falta de imagens	Imagem de difícil visualização	Legendas com informações ausentes	Informações não descritas, que necessitaram ser coletadas por meio da análise da imagem	Agrupamento de dados de uma série de casos, sem individualizar cada caso
Total (%)	36 (73,46)	23 (45,93)	24 (48,97)	13 (26,53)	5 (10,20)	23 (46,93)	16 (32,65)

O anexo B demonstra o número de casos e artigos por país. Uma maior quantidade de artigos e casos ocorreu nos Estados Unidos, sendo 19 artigos publicados e 56,03% do total de 539 casos estudados.

Discussão

Esse artigo mostra, pela primeira vez na literatura, uma revisão sistemática acerca das características epidemiológicas e clinico-histopatológicas do fibroma odontogênico periférico, contemplando 539 casos relatados. Os principais achados foram predominância em: 2ª e 4ª década de vida, mulheres, da etnia branca, lesão sintomática ou não, com tempo de evolução médio de 3,04 anos, localizando em gengiva mandibular, em região posterior ou anterior, e clinicamente apresentando-se como nódulo, ulcerado ou não, séssil, vermelho, de superfície lisa ou lobulada, e tamanho médio de 1,71cm. Os achados histológicos predominantes foram não ulceração do epitélio superficial, tecido conjuntivo fibrocelular, podendo ou não

apresentar calcificações (osso e cementóide principalmente), lesão não encapsulada, com a presença abundante ou escassa de ilhas e cordões de epitélio odontogênico.

Comparativamente aos dados apresentados pela OMS (2017) que relata que o FOP ocorre duas vezes mais em mulheres do que em homens, verificamos no presente estudo uma proporção de 1,44: 1 mulheres/ homens. O pico etário de idade entre a 2ª e 4ª décadas de vida foi condizente ao encontrado no presente estudo. Além disso, descreve a lesão como uma massa gengival séssil o que é compatível com a grande frequência de nódulos e aumento de volume relatados nos artigos verificados. Com referência a mucosa de superfície da lesão ser intacta, verificamos que pode ou não ser ulcerado. Quanto a ser localizada, na região anterior da gengiva, verificou-se que a lesão pode ocorrer tanto em região anterior quanto posterior com frequência similar.[1]

Em 85,90% dos casos, houve a presença de epitélio odontogênico no tecido conjuntivo, enquanto 8,90% dos casos estudados não relataram a presença de epitélio odontogênico porém os autores afirmaram ser um FOP. A OMS (2017) cita que a quantidade de epitélio odontogênico pode ser variável e ainda reforça que o epitélio pode variar de totalmente ausente a ser uma característica conspícua.[1] Apesar deste conceito, após o ano de 1985, todos os casos de FOP descritos na literatura relatavam a presença de ilhas ou cordões de epitélio odontogênico na sua composição histológica. Isso vem ao encontro de Daley & Wysocki (1994) que postularam que ambos os elementos, epitelial e mesenquimal são requeridos para o diagnóstico. Além disso, a ausência do epitélio odontogênico, dificulta o diagnóstico do fibroma periférico como de origem odontogênica.[2] Diante disto o presente estudo sugere que mais reflexões sejam conduzidas neste sentido. Apesar da classificação da OMS (2017) definir o epitélio do FOP como de aparência inativa, 0,93% do total de casos, o epitélio odontogênico era semelhante a ameloblastoma. É relatado que em alguns casos, a proliferação do epitélio odontogênico no FOP é tão marcante que pode ser difícil distinguir a lesão do ameloblastoma periférico. Esta proliferação associada a um envolvimento da mucosa superficial como observado em dois casos relatados por Siar & Han (1996) favoreceria o diagnóstico de ameloblastoma periférico. Entretanto, esses autores afirmam que o pequeno tamanho dessas lesões e confinamento do componente odontogênico epitelial, nas áreas periféricas dos tumores e ausência de

invasão nos tecidos moles adjacentes e no osso subjacente são achados que favorecem o diagnóstico de FOP.[28]

Um dos maiores desafios da etapa de busca por artigos foi a determinação das palavras-chave. A palavra-chave “fibroma odontogênico periférico” não está indexada no MESH, o que tornou necessário a inclusão do termo MESH “Odontogenic Tumors’’. Com isso, a busca tornou-se muito ampla, e mesmo condicionando a presença de termos como fibroma, associados à epitélio odontogênico, ilhas ou ninhos ou histopatológico, acabou abrangendo um grande número de lesões odontogênicas que não o FOP. Caso não houvéssemos incluído na busca essa expressão “Odontogenic tumors”, não haveríamos encontrados 10 (20,40%) dos 49 artigos eleitos. Isto demonstra, que é necessário associar à palavra-chave, um termo MESH, quando a lesão não se encontra indexada nessa base, mesmo que este amplie o número de artigos da busca inicial. Em uma revisão sistemática anterior realizada com outra lesão, demonstrou que o uso do termo MESH associado a uma palavra-chave, separadas pelas expressões boleanas E/OU, tiveram sua busca mais eficiente,[13] sendo esse o mesmo efeito na presente revisão sistemática.

No momento de extração de dados, surgiram novos desafios: dados clínicos e histopatológicos incompletos, falta de imagens, imagens de difícil visualização, legendas com informações ausentes, informações não descritas que necessitaram ser coletadas por meio da análise da imagem, agrupamento de dados de uma série de casos, sem individualizar cada caso. A única informação presente em 100% dos casos, foi idade, e para as demais observou-se uma variação na ausência de informação de 0,75 à 99,45%. Isto limita a precisão da identificação das características do FOP no presente estudo. Esses achados revelam a limitação do presente estudo e ressaltam a importância de se contemplar todas as características de uma lesão no momento de elaboração de um caso clínico ou série de casos. A ausência de informações em artigos de relatos e séries de casos foi descrita em artigos prévios.[11] Esses achados, revelam a necessidade de um maior rigor científico na qualidade dos relatos e séries de caso.

Com relação a falta de imagens, imagens de difícil visualização, legendas com informações ausentes, estes pontos dificultam a visualização do caso clínico, portanto, o presente estudo destaca que esses aspectos sejam observados tanto no momento da elaboração do artigo, quanto no momento da revisão desses artigos quando esses

são submetidos para avaliação das revistas. A maior prova da importância de ser acrescentado as imagens do caso, é que, algumas informações pontuais, como por exemplo, lesão fundamental, cor, inserção, que não estavam contidas na forma escrita do texto, foram coletadas por meio da análise da imagem, o que ocorreu em 23 artigos.

Os artigos de séries de casos, não individualizaram as características de cada caso, revelando a frequência de cada característica na amostra, o que levou a os autores da presente revisão sistemática a considerar a média em algumas situações, como a idade dos indivíduos, tempo de evolução e o tamanho da lesão. O presente estudo alerta que posteriores artigos de séries de casos, mostrem as características das lesões, individualizadas, caso a caso, se possível no artigo ou como material suplementar.

Portanto, o presente estudo ressalta uma padronização ao se descrever um caso clínico, uma série de casos ou um estudo epidemiológico contemplem todos as variáveis clínicas-epidemiológico e histológicas possíveis. Dos artigos analisados, 28 eram de estudo de caso e 21 eram de série de caso. Não foi incluso na presente revisão sistemática um artigo que avaliou comparativamente, por meio da imuno-histoquímica para PCNA e a técnica de AgNORs, o FOP com a variante central e com fibroma ossificante, pois a caracterização epidemiológica, clínica e histopatológica da amostra não foi revelada neste artigo.[60] Estes 49 artigos inclusos no presente estudo, associados com esse último, revelam que a literatura sobre o fibroma odontogênico periférico é carente de trabalhos com maior nível de evidência científica, como uma revisão sistemática.

Conclusão

A literatura exibe estudos e relatos de caso descrevendo as características da lesão de forma incompleta, sendo todos eles relatos ou série de casos, sendo carente de trabalhos com maior nível de evidência científica, como uma revisão sistemática, além de necessitar de um maior rigor científico na qualidade desses artigos. Mesmo assim, dentro das limitações, foi possível identificar que o fibroma odontogênico periférico é mais comum em mulheres brancas, entre as segundas e quarta décadas,

caracterizado como nódulo vermelho na região posterior e anterior da mandíbula, com superfície lisa ou lobulada.

Conflitos de interesse: não houve conflitos de interesse.

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Title Page

Title: Peripheral odontogenic fibroma: a systematic review

Authors:

1. André Tschoeke, DDS
2. Aline Cristina Batista Johann, DDS, MSc, PhD

Institutional Affiliation:

[a]Pontifical Catholic University of Paraná, Imaculada Conceição Street, 1155, Prado Velho 80.215-901, Curitiba, PR, Brazil.

Corresponding author:

Professor Aline Cristina Batista Rodrigues Johann. PhD
School of Dentistry
Pontifical Catholic University of Paraná
Imaculada Conceição Street, 1155, Prado Velho 80.215-901 Curitiba, PR, Brazil.
Phone: +55 41 3271-2592 Fax: +55 41 3271-1405
E-mail: alinecristinabatista@yahoo.com.br

Word Counting: 2231

Abstract: 335

Figures: 1

Tables: 5

References: 69

Main finding: It was verified, from the systematic review, that the literature about peripheral odontogenic fibroma is poor in researches with a greater level of scientific

evidence, as a systematic review, and needs a greater scientific rigor in quality of the reports and series of case.

Abstract

Introduction: Peripheral odontogenic fibroma (POF) is a benign mesenchymal odontogenic neoplasia characterized as a tough gingival mass, usually sessile and similar in color to the normal mucosa. Researches have been describing this lesion in an isolate way, without grouping information, which made it necessary the elaboration of a systematic review to identify the predominant characteristics of this lesion, being the objective of the present study. **Methods:** It was included articles in English, with humans, with histological diagnosis of POF, containing at least one of the epidemiological, clinical and histological characteristics. The search for articles, and extraction of data were conducted independently and in duplicate and the search of publications with keywords, in Pubmed, VHL, Cochrane, Science Direct and Scopus databases, including articles inserted until November 2016. **Results:** From 964 articles, 908 were excluded after applying the eligibility criteria, with 49 being eligible, 28 being case reports and 21 case studies. Of these articles, 539 case reports were from patients presenting POF. The most frequent epidemiological characteristics were white women between the 2nd and 4th decade of life. The lesion's average evolution time was 3,04 years. Clinically, it predominates in posterior or anterior mandibular gums, as a nodule, ulcerated or not, and sessile. The main histopathological findings were absence of ulceration of the superficial epithelium, fibrocellular connective tissue, presenting or not presenting calcifications, non-encapsulated lesion, with abundant or scarce presence of islands and cords of odontogenic epithelium. In some articles there were lack of information, lack of images, images difficult to visualize, missing information labels, information that needed to be collected through the image and data grouping. **Conclusion:** The literature shows few articles describing the characteristics of the lesion, most of them incomplete. This issue needs more papers with higher level of scientific evidence, as a systematic review, requiring a greater scientific rigor in the quality of these articles. Within limitations, it was possible to identify predominant

characteristics of POF and that the presence of odontogenic epithelium to define the lesion histologically needs to be evaluated.

Key-words: Odontogenic Tumor, Fibroma, Human

Introduction

Odontogenic fibroma is described by the World Health Organization (WHO) in 2017 as “a rare benign mesenchymal odontogenic tumor with variable amount of inactive-looking odontogenic epithelium with or without evidence of calcification”. This lesion can be found either inside the jaw bones or can be found in the buccal mucosa. [1]Peripheral Odontogenic Fibroma (POF) is considered the extra bone equivalent of Central Odontogenic Fibroma. [1-2]The first article reporting a case of peripheral odontogenic fibroma is from 1958,[3] and since then, studies have been conducted, but no systematic review has been done.

Clinically, POF presents as a tough gingival mass, usually sessile, with slow, painless growth and similar color to adjacent mucosa.[2,4,5] Radiographically, POF may have areas of radiopacity but does not affect the adjacent bone. [2] The clinical differential diagnoses of POF are inflammatory fibrous hyperplasia, fibroma, peripheral ossifying fibroma, peripheral giant cell granuloma, and pyogenic granuloma.[7] The treatment is local excision of the lesion, and the prognosis is excellent with rare recurrences.[4,5]

Studies and case reports have been describing this lesion in an isolated form, without grouping the information. It is important to report this lesion, so that the variations of its characteristics can be shown and it would help to establish the correct diagnosis, histopathology, treatment options and the recurrence rate (Reddy et al. 2014). In addition, it is essential to group this information with accuracy, so that a systematic review is necessary to determine the predominant epidemiological, clinical and histological characteristics of this lesion, since published literature show gaps in the diagnostic areas, [9] being this the purpose of the present study, which may help the dentist’s conduct in similar cases. Systematic reviews help professionals to update themselves, summarizing large studies and discussing the difference from their point of view on a certain topic [6]. Systematic reviews of clinical and radiographic features of

oral and maxillary lesions have been conducted in: melanoacanthoma [10], inflammatory fibrous hyperplasia, [9] lymphoma, [10] odontogenic keratocystic tumor, [11] orthokeratinized odontogenic cyst, [12] and odontogenic glandular cyst.

The objective of the study was to identify the epidemiological, clinical and histological characteristics of POF, by a systematic review.

Methods

Systematic Review

The protocol of systematic review was based on the criteria presented by *Preferred Reporting Items for Systematic Reviews and Meta-Analyses*, o PRISMA.[25]

Clinically relevant question: What is the epidemiological, clinical and histological profile of POF?

Inclusion Criteria: Articles in English, with (human) individuals with histological diagnosis of POF and with, at least, one of each epidemiological, clinical and histological characteristic.

Exclusion Criteria: Literature review and articles that did not define the type of lesion (central or peripheral/odontogenic fibroma or ossifying fibroma).

Data sources: The search was made in the National Library of Medicine (NLM-interface PubMed), and the Virtual Health Library (VHL), Cochrane, Science Direct and Scopus, included in the platforms until the month of November 2016.

Terms used to search on PubMed (Annex F): (((Peripheral odontogenic fibroma) OR ((((("Odontogenic Tumors"[Mesh]) AND "Fibroma"[Mesh])) AND ((((("Diagnosis"[Mesh]) OR odontogenic epithelium[Title/Abstract]) OR (nets[Title/Abstract] OR islands[Title/Abstract]) OR histopathology)) AND ((((((((((("Gender Identity"[Mesh]) OR "Sex"[Mesh]) OR male[Title/Abstract]) OR female[Title/Abstract]) OR man[Title/Abstract]) OR woman[Title/Abstract])) OR (((((("Age of Onset"[Mesh]) OR years[Title/Abstract]) OR Onset Age[Title/Abstract]) OR Age-at-Onset[Title/Abstract]) OR Age at Onset[Title/Abstract])) OR (((((((("Disease Attributes"[Mesh]) OR clinical characteristics[Title/Abstract]) OR Attribute, Disease[Title/Abstract]) OR Attributes, Disease[Title/Abstract]) OR Disease Attribute[Title/Abstract]) OR nodule[Title/Abstract]) OR sessile[Title/Abstract]) OR pedicellate[Title/Abstract]) OR gingival mass[Title/Abstract]))) OR "Humans"[Mesh])))

The search for articles, and data extraction were conducted independently and in duplicate. A third evaluator solved the differences on the cases. Initially, articles were withdrawn in duplicate, followed by deletion of articles that did not attend the eligibility criteria. The articles were tabulated in Excel, following the process of data extraction, including information regarding the articles: a) authorship, year of publication, number of cases; b) epidemiological aspects: ethnicity and gender of participants, age; c) Anamnesis: signs and symptoms, time of evolution; d) Clinical aspects: location, fundamental lesion, ulceration, insertion, color, surface, size, dental displacement; e) histopathological aspects were odontogenic epithelium islands or cords, quantity, ameloblastoma-like epithelium, epithelium with differential for light cells, connective tissue type, superficial epithelial ulceration, basal cells in buds, presence of calcification, lesion encapsulated; f) recurrence.

To classify the patients in decades, the mean age was made and converted into decades. For the evolution of the lesion, the average number of cases per article was obtained, and for the calculation of the size, the average was performed in cm per article.

Results

A total of 964 articles were found, of which 895 were excluded because they were not articles about POF and 1 article was excluded for doing an immunohistochemical study comparing with other lesions and not characterizing epidemiologically, clinically and histopathologically. Another 15 were excluded because they were articles found in other languages than English and 11 because they could not be found, even after requesting authors, bibliographic switching and attempted purchase, totaling 907 articles excluded in this stage of screening. The complete texts of 58 articles were read, and 9 were excluded because they were a review of the literature, two of peripheral fibroma (without determining whether it was odontogenic or ossificant), or ossifying peripheral fibroma, or for not showing at least one of each epidemiological, clinical and histological characteristics. Annex A show the excluded articles at this stage, with its respective reasons. A total of 49 studies fulfilled inclusion criteria, of these 28 articles were case reports and 21 articles with case series. Flowchart 1 illustrates this process of article selection.

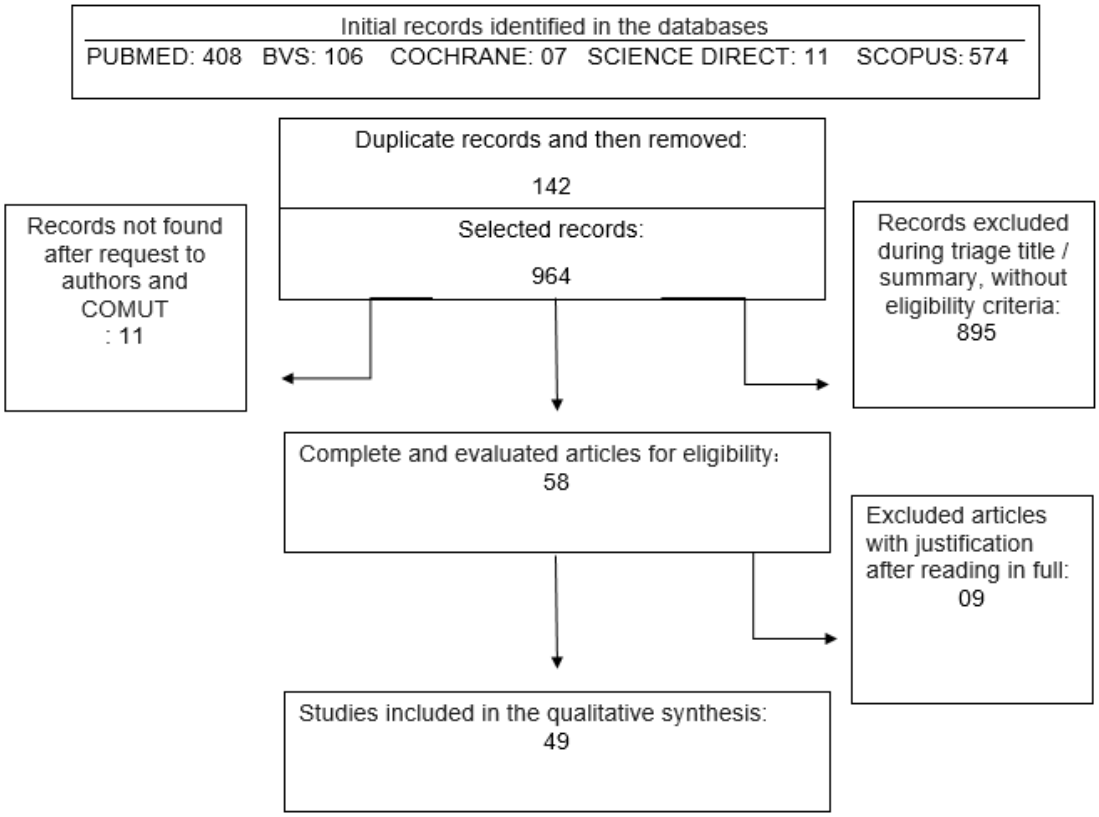

Figure 1. Flowchart for article selection

Of the 49 articles, 539 cases of patients with POF were identified. Table 1 shows authorships, number of cases per article, epidemiological characteristics, signs and symptoms and time of evolution of POF. The tables are arranged by the clinical (table 2) and histological (tables 3 and 4) characteristics found in the systematic review. In Annex C, the clinical and histological characteristics are distributed according to the article from which they were extracted. In all the cases the cirurgical excision was the treatment option and the recurrence rate was 10,58% of the cases, while 66,41% of the cases did not show recurrence. In 23,01% of the cases, this information was not cited.

Table 1. Authorship, year of publication, number of cases, age, sex, ethnicity of individuals, signs and effects of time of evolution in cases of peripheral odontogenic fibroma.

References	Year	Number of cases	Age (Decade)	Sex	Ethnicity	Signals and symptons	Evolution (years)
Buckman[3]	1958	1	6ª	F	Y	*	14
Farman[15]	1975	10	Average3ª	6M/4F	9B/1W	10*	*
Lownie et al.[4]	1976	1	4ª	F	B	No	0,16
McGuff et al. [16]	1981	1	2ª	M	W	No	0,33
Klein[17]	1982	1	3ª	M	W	*	0,16
Harisson et al.[18]	1983	1	2ª	F	*	*	3
Pockrass et al.[19]	1983	1	7ª	F	W	*	*
Mulcahy & Dahl[20]	1985	52	Average4ª	13M/39F	47W/5*	52*	Average3,75
McGnnis & Ray[21]	1985	1	3ª	F	W	No	2
Buchner et al.[5]	1987	9	Average5ª	5M/4F	6W/2B/1Y	Bleeding: 1/ 8*	Average0,55
Buchner[22]	1989	5	Average4ª	2M/3F	5*	5*	Average0,775
Kenney et al[23]	1989	13	Average2ª	8M/5F	8W/4B/1*	13*	*
Slabbert & Altini[24]	1991	30	Average3ª	16M/12F/2*	28B/2*	30*	*
Michaelides[7]	1992	1	6ª	F	W	No	0,08
Weber et al[25]	1992	3	Average3ª	1M/2F	2B/1W	3*	Average3
Ficarra et al[8]	1993	1	2ª	F	Wh	*	*
Daley & Wysocki[27]	1994	36	Average4ª	12M/24F	14W/1B/21*	No: 7/ 29 *	Average2,24
Siar& Ng[28]	1995	2	Average4ª	1M/1F	2Y	2*	Average1
Siar& Ng[29]	1995	1	7ª	F	Y	*	0,33
Siar& Ng[30]	2000	46	Average4ª	20M/26F	46*	Pain, Bleeding: 16 / 30*	Average2
Flaitz[31]	2001	1	2ª	M	B	No	*
Manor et al[32]	2004	2	4ª	*	2*	2*	*
Martelli-Júnior et al[33]	2006	1	1ª	F	W	*	0,33
Buchner et al.[34]	2006	23	Average4ª	11M/12F	19W/2B/1Y	23*	*
Bonetti et al[35]	2006	1	2ª	M	W	*	3
Bosco et al[36]	2006	1	2ª	F	W	Discomfort	0,5
Garcia et al.[37]	2007	17	4ª	2M/15F	11W/2B/4*	No: 4/13*	*
Rinaggio et al[38]	2007	1	6ª	F	*	No	0,16
Lin et al[39]	2008	25	Average4ª	9M/16F	25Y	25*	*
Ide et al[40]	2008	1	2ª	1F	Y	*	3
Alaeddini et al[41]	2010	19	Average 4ª	11M/8F	19*	19*	*
Ritwik & Brannon [42]	2010	151	Average4ª	65M/86F	97W/46B/8*	151*	Average20
Ramachandra et al[43]	2011	1	2ª	M	*	*	10
Baiju & Rohatgi[59]	2011	1	3ª	F	*	*	1
Brooks&Nikitakis[44]	2011	1	3ª	F	W	Bleeding	6
Patel et al[45]	2011	1	4ª	M	W	No	*
Eversole [46]	2011	40	4ª	13M/27F	40*	40*	*
Lin et al[47]	2011	12	4ª	6M/6F	12*	12No	Average1,5
Silva et al[48]	2012	1	2ª	F	W	No	1
Wood et al[49]	2012	1	7ª	F	*	*	*
Livada et al[50]	2013	1	3ª	M	B	No	2
Wu et al [51]	2013	10	Average4ª	7M/3F	10*	10*	*
Soileau[52]	2013	1	6ª	F	B	*	10
Reddy et al [53]	2014	1	5ª	F	B	*	1
Sreeja et al[54]	2014	1	6ª	M	B	No	0,5
Kumar et al[55]	2014	1	3ª	F	*	*	5
Truschnegg et al[56]	2015	3	Average3ª	3F	3*	3*	*
Silva et al[57]	2016	3	Average3ª	2M/1F	1W/1B/1Br	3No	Average1,47
Bharathi et al. [58]	2016	1	6ª	M	*	No	0,5
Total (%)		539	1ª: 2,05 2ª:20,40 3ª:22,45 4ª:32,65 5ª:4,08 6ª:12,25 7ª:6,12	219(40,63) M 316(58,62) F 4(0,75)*	218(40,45) W 107(19,85) B 32(5,94) Y 1(0,18) Br 181(33,58) *	19(3,52)Symptons 26(4,83) No 494(91,65) *	Average: 3,04 years

Subtitle: M= male, F= female, Y= yellow, W= white, B= black, Br= Brown, *= not reported

Table 2. Variable, number of cases, location, jaw involved, region, fundamental lesion, presence of ulceration, insertion, color, surface, evolution, size, signs and symptoms, dental displacement and differential diagnosis in cases of peripheral odontogenic fibroma.

Variable/ total (%)	Location	Maxilla or mandible	Region	Lesion	Ulcerated	Insertion	Color	Surface	Size (cm)	Tooth dislocation
								20(3,72) Sm		
	8 (1,49) AR	257(47,69) Md	92(17,06) Posterior				5(0,93)P	12(2,22)		14(2,60) Yes
	495 (91,84)G	190(35,25) Mx	82(15,40)	213(39,52)N	74(13,73)Yes	192(35,62)S	112(20,77)R	Lo		65(12,05)No
	36 (6,67)*	92(17,06) *	Anterior	111(20,60) I	86(15,95)No	93(17,25)P	42(7,80)SM	507(94,06)	Average	460(85,35)*
539			364(67,54)*	196(39,88)*	379(70,32)*	254(47,13) *	380(70,50)*	*	size= 1,71	

Subtitles: AR= Alveolar ridge, G= Gum, Md= Mandible, Mx= Maxilla, I= Increase of volume, N= Nodule, S= Sessile, P= Pediculated, P= Pink, R= Red, SM= Similar to mucosa, Lo= Lobed, Sm= Smooth
*=No relatated

Table 3: Variable, number of cases, degree of surface epithelium ulceration, connective tissue type, presence of calcifications / bone / dentin, presence of capsule in peripheral odontogenic fibroma.

Variable/ total (%)	Degree of surface epithelium ulceration	Connective tissue type	Calcification	Bone	Cement	Dentin	Dystrophic calcification	Capsule
	132(24,48) NU /28(5,20)MOD/	220(40,82) FC/ 146(27,08) MX/	234(43,41)No					2(0,37) Yes
539	12(2,23) EU/ 367(68,09)*	14(2,60) HF/ 159(29,50)*	248(46,01)Yes 57(10,58)*	116(21,52)Yes 423(78,48)*	118(21,89) Yes 421(78,11)*	28(5,20) Yes 511(94,80)*	42(7,80) Yes 496(92,20)*	102(18,92) No 435(80,71)*

Subtitles: NU= Not ulcerated Mod= moderate, EU= extensively ulcerated, FC= fibrocellular, MX= myxoide, FH= hyalinized fibrous, *=Not informed

Table 4- Variable, number of cases, islands and cords of odontogenic epithelium, amount, epithelium, ameloblastoma, epithelium with differential for clear cells, basal cells in shoots, immunopositivity of odontogenic epithelium of peripheral odontogenic fibromas.

Variable / total (%)	Islands and cords of odontogenic epithelium	Amount	Ameloblastoma-like epithelium	Epithelium with differential for clear cells	Basais cells in shoots
		74(13,73) Abundant			
	463(85,90) Yes	39(7,24) Moderate			
539	48(8,90) No	74(13,73)Scarce	5(0,93) Yes	3(0,55) Yes	39(7,23) Yes
	28(5,20)*	352(65,30)*	534(99,07)*	535(99,45)*	500(92,77)*

*= Not informed

Table 5 show the main difficulties found in the moment of data extraction and analysis and in the annex D, the mains difficulties are disposed according with its original article.

Table 5- Difficulties found each article

Ref.	Incomplete clinical data	Incomplete histopathological data	Lack of images	Difficult to see image	Subtitles with missing information	Information not described, which needed to be collected through image analysis	Grouping of data in a serie of cases, without individualizing each case
Total (%)	36 (73,46)	23 (45,93)	24 (48,97)	13 (26,53)	5 (10,20)	23 (46,93)	16 (32,65)

Annex B show the number of cases and articles per country. The most part of articles and cases were from the United States of America, being 19 published articles and 56,03% from the total of cases studied (539).

Discussion

This article shows, for the first time in the literature, a systematic review about the epidemiological, clinical and histopathological characteristics of the peripheral odontogenic fibroma, including 539 cases. The main findings were predominance in: 2nd and 4th decade of life, white women, symptomatic or not, with an average evolution time of 3,04 years, located in mandibular gums, posterior or anterior region, and clinical characteristics of nodule, ulcerated or not, sessile, red, smooth or lobed surface, and average size 1.71cm. The predominant histological findings were non-superficial epithelial ulceration, fibrocellular connective tissue, presenting or not calcifications (bone and mainly cementoid), non-encapsulated lesion, with abundant or sparse presence of islands and cords of odontogenic epithelium.

Comparing to WHO data presented in 2017, that says POF occurs twice times more in women than in men, we verified in this review a proportion of 1,44: 1 women/men. The peak age is between 2nd and 4th decades of life was the same of this study. It also describes the lesion as a sessile gingival mass that is compatible with the great frequency of nodules and increased volume showed by the read articles. About the surface of the lesion being intact we verified that it can be or not ulcerated. About the location, on the anterior region of gums, it was verified that the lesion may occur both anterior or posterior region with similar frequency.

In 85.90% of the articles, odontogenic epithelium was present in connective tissue, while 8,90% of the articles studied did not report the presence of odontogenic epithelium, but the authors declared that it was a POF. WHO (2017) affirms that the amout of odontogenic epithelium can be variable and reinforces that the epithelium may vary from totally absence till being conspicuous characteristic[1]. It corroborates with Daley & Wysocki (1994) that says that both epithelial and mesenchymal elements are required for diagnosis. Besides this, the absence of odontogenic epithelium difficulties the diagnosis of peripheral fibroma as odontogenic origin[2]. So, we suggest that more studies should be done about this. Despite WHO classification (2017), that defines POF epithelium as inactive-looking, 0,93% of the cases the odontogenic epithelium looked like ameloblastoma. In some cases, the proliferation of odontogenic epithelium is so strong that is difficult to distinguish from peripheral ameloblastoma. This proliferation, associated with the involvement of the superficial mucosa, as observed in two cases reported by Siar & Han (1996), is favorable to peripheral ameloblastoma diagnosis. However, the authors state that the small size of the lesions and confinement of epithelial odontogenic compound in peripheral region of the tumors and the absence of invasion in adjacent soft tissues and underlying bone are findings that favor POF diagnoses.

One of the major challenges of the search for articles was to determinate the keywords. The key word "peripheral odontogenic fibroma" is not indexed on MESH, which made necessary to include the term MESH "odontogenic tumors". Thus, the search became very broad, and even conditioning terms like fibroma, associated with odontogenic epithelium, islands or cords or histopathological, ended up covering a large number of odontogenic lesions other than POF. If there were not included in the search for the term "odontogenic tumors", 10 (20,40%) of the 49 articles would be not found. This demonstrates that it is necessary to associate the keyword with a MESH term, when one is not found in a database, even if it expands the number of initial search articles. In an earlier systematic review about other lesion, it has been shown that the use of the term MESH associated with a keyword, separated for Boolean expressions AND / OR, fears its more efficient search, [13] being this same effect in the present systematic review.

At the moment of data extraction, new challenges arose: incomplete clinical and histopathological data, lack of images, images difficult to visualize, missing information

captions, non-described information that needed to be collected through image analysis, series of cases, without identifying each case. The only information present in 100% of the cases was age, and for the others, there was a variation in the absence of information from 0.75 to 99.45%. It limits the identification precision of the POF characteristics. These findings reveal the limitation of the present study and emphasize the importance of considering all the characteristics of an injury at the moment of elaboration of a clinical case or series of cases. The lack of information in articles of reports and series of cases was described in previous articles.[11] These findings reveal the need for greater scientific rigor in the quality of case reports and case series.

Regarding the lack of images, images difficult to visualize, subtitles with missing information, these points make it difficult to view the clinical case, therefore, the present study highlights that these aspects are observed both at the time of writing the article and at the moment of the review when they are submitted for evaluation of journals. The greatest proof of the importance of adding the images of the case is that some punctual information that was not in the written form of the text was collected through image analysis, which occurred in 23 articles.

The articles of case series did not individualize the characteristics of each case, revealing the frequency of each characteristic in the sample, which led the authors of the present systematic review to consider the average in some situations, such as age, time evolution and size of the lesion. The present study alerts that further articles in case series show the characteristics of the lesions, individualized, case by case, if possible in the article or as supplementary material.

Therefore, the present study highlights standardization when describing a clinical case, a series of cases or an epidemiological study containing all possible clinical-epidemiological and histological variables. Of the articles analyzed, 28 were case study and 21 were case series. It was not included in this systematic review an article that comparatively evaluated, through immunohistochemistry for PCNA and AgNORs' technique, POF with the central variant and ossifying fibroma, because the epidemiological, clinical and histopathological characterization of the sample of this article was not revealed [60]. These 49 articles included in this study, associated with this last one mentioned, reveal that the literature on peripheral odontogenic fibroma is poor in papers with a higher level of scientific evidence, such as a systematic review.

Conclusion

The literature shows few papers describing incomplete characteristic of the lesion, being all reports or series of cases, revealing lack of articles with a higher level of scientific evidence, such as a systematic review, besides the need for a greater scientific rigor in the quality of this articles. Anyway, within these limitations, it was possible to identify peripheral odontogenic fibroma is more common in white women, between 2nd and 4th decade of life, characterized as red nodule on both posterior and anterior region of de mandibule, with lobulated or smooth surface.

Conflict of interests: the authors declare no conflict of interests.

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ANEXO A: Artigos excluídos com justificativa

Referência e ano	Motivos de eliminação
Anand et al., 1967	Não houve definição se o fibroma periférico era de natureza odontogênica ou ossificante
Schneider&Weisinger, 1978	Não apresentou dados epidemiológicos e clínicos
Wright&Jennings, 1979	Não apresentou dados epidemiológicos, clínicos e histopatológicos
Gorrel&Larsson, 1983	Não apresentou dados epidemiológicos e clínicos
Wescott, 1983	Não apresentou dados epidemiológicos, clínicos e histopatológicos
Williams et al., 1984	Não apresentou dados epidemiológicos, clínicos e histopatológicos
Doyle et al., 1985	Não ficou claro se o caso de fibroma odontogênico era intraósseo ou extra ósseo
Kimberley&Marentette, 1988	Não apresentou dados histopatológicos do caso, somente dados da literatura
Ide et al., 2005	Não apresentou dados epidemiológicos, clínicos e histopatológicos

ANEXO B: Número de casos e artigos por país.

País	Nº de artigos com casos de FOP	Nº de casos de FOP por país	% nº casos
Estados Unidos	19	302	56,03
Índia	6	6	1,11
Brasil	5	23	4,26
África do Sul	5	45	8,35
Taiwan	3	47	8,74
Malásia	3	49	9,1
Itália	1	1	0,18
Grécia	1	1	0,18
Irã	1	19	3,53
Canadá	2	37	6,86
Israel	1	5	0,93
Aústria	1	3	0,55
Japão	1	1	0,18
Soma	49	539	100

ANEXO C- Tabelas discriminando características epidemiológicas, clínicas e histológicas por artigo.

Tabela 2. Referência, número de casos, localização, maxilar envolvido, região, lesão fundamental, presença de ulceração, inserção, cor, superfície, evolução, tamanho, sinais e sintomas, deslocamento dentário e diagnóstico diferencial em casos de Fibroma odontogênico periférico.

Ref/ casos	Localização	Maxila ou mandíbula	Região	Lesão	Ulcerado	Inserção	Cor	Superfície	Tamanho (cm)	Deslocamento dentário
3/1	RA	Md.	Anterior	A	Não	S	R	Lo	3,5	Sim
15/10	10G	10Md.	10Posterior	10A	1Sim/9 não	10S	10*	10*	Média 2,75	3Sim/7Não
4/1	G	Mx.	Posterior	A	*	P	*	*	1	*
16/1	G	Mx.	Anterior	A	Sim	P	*	*	0,5	Não
17/1	G	Mx.	Anterior	N	Sim	P	R	Lo	1	*
18/1	RA	Mx	Anterior	N	*	P	V	Lo	1	*
19/1	52G	52*	Anterior	A	Não	P	*	Li	*	*
20/52	G	Md.	52*	52*	52 Sim	52P	52 V	52*	*	1Sim/51*
21/1	9G	6Md/3Mx.	Anterior	A	Não	S	*	*	0,8	Não
5/9	2RA/2G	3Md/2Mx.	8Posterior/ 1Anterior	2N/7A	2Sim/7não	6S/2P/1*	3 V, 6*	9*	Média 0,8	9*
22/5	13G	9Md/4Mx	5Posterior	5 A	5*	5*	5 V	5 Li	Média 1,34	5*
23/13	30G	16Md/14Mx.	8Posterior/ 5Anterior	13*	13*	13*	13*	13*	*	13*
24/30	G	Mx.	30*	30*	30*	30P	30 SM	30*	Média 2	30*
7/1	3G	3Mx.	Anterior	A	Sim	S	*	Lo	1,4	*
25/3	G	Mx.	3Anterior	2N/1*	3Não	3S	3 SM	2 Lo/1 Li	*	3*
8/1	36G	36*	Anterior	N	*	*	*	*	*	*
27/36	2G	2Mx.	36* *	1N/6ª/29	36*	36*	36*	1Lo/35*	Média 0,8	36*
28/2	G	Md.	2Anterior	1N/1A	2*	2P	2*	2*	*	2*
29/1	46G	24Md/20Mx.	Posterior	A	*	*	*	*	*	*
30/46	G	Md.	46*	4N/42A	3Sim/43Não	46*	46*	46*	*	2Sim/44*
31/1	G	2Md.	Posterior	A	Não	S	R	Li	2	Não
32/2	RA	Mx.	2*	2*	2*	2*	2*	2*	Média 1	2*
33/1	3RA/20G	16Md/7Mx	*	A	Não	S	R	Li	1	Não
34/23	RA	Md.	12Posterior /11Anterior	23*	23*	23*	23*	23*	Média 0,8	23*
35/1	G	Mx.	Posterior	A	*	S	SM	*	4	Sim
36/1	17*	10Md/5Mx/2*	Posterior	N	Sim	S	V	Lo	1	*
37/17	G	Md.	9Posterior/ 6Anterior	17*	17*	17*	17*	17*	1,55	17*
38/1	25G	11Md/14Mx	Anterior	N	Não	P	SM	Li	0,4	*
39/25	G	Mx	25*	25*	25*	25*	25*	25*	Média 1,2	1Sim/24*
40/1	19*	11Md/6Mx/1*	Anterior	A	Não	S	SM	Li	*	*
41/19	151G	88Md/63Mx	19*	19*	19*	19*	19*	19*	*	19*
42/151	G	Mx	151*	151N	151*	151S	151*	151*	Média 1,2	151*
43/1	G	Md	Anterior	A	Não	S	SM	Li	4	Sim
59/1	G	Mx	Posterior	A	Não	S	SM	Li	1	Sim
44/1	G	Mx	Anterior	N	Não	*	SM	Li	*	*
45/1	40G	23Md/17Mx	Posterior	N	Sim	S	V	Lo	2	*
46/40	1RA/24G	8Md/4Mx	17Posterior/ 23Anterior	40N	40*	40*	40V	40*	*	40*
47/12	G	Md	5Posterior/ 7Anterior	12A	7Sim/5Não	12*	12*	12*	Média 1,9	12*
48/1			Anterior	N	Sim	S	V	Li	*	*

49/1	G	Mx	Anterior	A	Não	S	V	Lo	*	*
50/1	G	Mx	Anterior	A	Não	S	V	Li	1,2	Não
51/10	10G	6Md/4Mx	4Posterior/ 6Anterior	10A	10*	10*	10*	10*	Média 1,5	10*
52/1	G	Mx	Anterior	N	Não	S	V	Li	1	*
53/1	G	Mx	Posterior	A	Sim	S	V	Lo	4	Sim
54/1	G	Mx	Posterior	A	Sim	S	V	Lo	3	Sim
55/1	G	Mx	Anterior	A	Não	S	R	Li	4	Sim
56/3	3G	3Md	3Posterior	1N/2*	3*	1S/ 2*	3SM	1 Li/2*	*	3*
57/3	3G	1Md/2Mx	1Posterior/ 2Anterior	1N/2A	1Sim/2Não	3S	2 V/1*	1 Li/ 2*	Média 1,3	3*
58/1	G	Md	Posterior	A	Sim	P	V	Lo	2,5	Não
Total (%)	8 (1,49)RA 495 (91,84)G 36* (6,67)	257(47,69)Md 190(35,25) Mx 92 (17,06) *	92(17,06) Posterior 83(15,40) Anterior 364(67,54)*	213(39,52)N 111(20,60)A 215(39,88)*	74(13,73) Sim 86(15,95) Não 379(70,32)*	192(35,62)S 93(17,25)P 254 (47,13)*	5(0,93) R 112 (20,77)V 42 (7,80)SM 380(70,50)*	20(3,72) Li 12(2,22) Lo 507(94,06)*	Média tamanho= 1,71	14(2,60) Sim 65(12,05)Não 460(85,35)*

Legendas: RA= Rebordo Alveolar, G= Gengiva, Md= Mandíbula, Mx= Maxila, A= Aumento de volume, N= Nódulo, S= Séssil, P= Pediculado, R= Rosa, V= vermelho, SM= semelhante a mucosa, Lo= Lobulada, Li= Lisa *=Não relata.

Tabela 3. Referência, número de casos, grau de ulceração do epitélio de superfície, tipo de tecido conjuntivo, presença de calcificações/osso/dentina, presença de cápsula em Fibromas Odontogênicos periféricos

Ref./ Casos	Grau de ulceração do epitélio de superfície	Tipo de Tecido Conjuntivo	Calcificação	Osso	Cementóide	Dentina	Calcificação distrófica	Cápsula
3/1	NU	FC	1Sim	*	1Sim	1*	1*	1Sim
15/10	4MOD/6NU	7FC/3MX	2Não/4Sim/4*	2Sim/8*	2Sim/8*	10*	10*	10Não
4/1	*	FC	1Sim	1*	1*	1Sim	1*	*
16/1	*	FC	1Sim	1*	1Sim	1*	1*	*
17/1	MOD	FC	1Sim	1Sim	1Sim	1*	1*	1Sim
18/1	*	FC	1Sim	1Sim	1*	1*	1*	*
19/1	*	FC	1Sim	1Sim	*	*	*	*
20/52	20NU/32*	52FC	20Não/21Sim/ 11*	9Sim	12 Sim	52*	16/36*	52*
21/1	NU	FH	1Sim	1	1Sim	1*	1*	Não
5/9	2MOD/7NU	6FC/1MX/2FH	7Não/2Sim	9*	9*	9*	2Sim/7*	9*
22 /5	5*	4FC/1MX	5Sim	5*	5*	5Sim	3Sim/2*	5*
23/13	13*	13*	13*	13*	13*	13*	13*	13*
24/30	30*	30MX	8Não/22Sim	22 Sim	22Sim	30*		30*
7/1	MOD	FC	1Sim	1*	1*	1*	1Sim	*
25/3	3*	1FC/1MX/1FH	2Não/1Sim	3*	3*	3*	1Sim	3*
8/1	NU	FH	1Sim	1*	1*	1*	1Sim	*
27/36	36*	20FC/2MX/14*	22Não/14Sim	3 Sim/33*	7Sim/29*	7Sim/29*	36*	36*
28/2	2*	2FC	2Não	2*	2*	2*	2*	2*
29/1	NU	FC	1Não	1*	1*	1*	1*	Não
30/46	11EU/2MOD/33NU	19FC/5MX/2FH/20*	23Não/23Sim	13 Sim/33*	7Sim/39*	2Sim/44*	1Sim	46*
31/1	NU	MX	1Não	1*	1*	1*	1*	*
32/2	2*	2*	2*	2*	2*	2*	2*	2*
33/1	NU	MX	1Não	1*	1*	1*	1*	*
34/23	23*	23*	23*	23*	23*	23*	23*	23Não
35/1	*	MX	1Não	1*	1*	1*	1*	*
36/1	*	*	*	1*	1*	1*	1*	*
37/17	15NU/2MOD	12FC/1MX/4*	10Não/7Sim	6Sim/11*	1Sim/16*	17*	17*	17*
38/1	NU	FC	1Não	1*	1*	1*	1*	
39/25	1EU/ 24NU	25*	2Sim/23*	23*	1Sim/24*	1Sim/24*	25*	25 não
40/1	*	FC	Sim	Sim	*	Sim	*	Não
41/19	7MOD/12NU	17FC/1MX/1FH	5Não/14Sim	9Sim/10*	8Sim/11*	19*	19*	19*
42/151	151*	55FC/86MX/10*	61Não/90Sim	44Sim/107*	34Sim/117*	11Sim/140*	15Sim/136*	151*
43/1	NU	FC	1Não	1*	1*	1*	1*	*
59/1	MOD	MX	1Sim	1*	1Sim	1*	1*	*
44/1	*	FC	1Não	1*	1*	1*	1*	*
45/1	MOD	FC	1Sim	1*	1*	1*	1Sim	*
46/40	40*	40*	40*	40*	40*	40*	40*	40Não
47/12	7MOD/5NU	9FC/3MX	12Sim	8Sim/4*	4Sim/8*	12*	12*	12*
48/1	MOD	MX	1Sim	1*	1*	1*	1*	*
49/1	*	FC	1Sim	1*	1*	1*	1Sim	*
50/1	*	FC	1Não	1*	1*	1*		*
51/10	10*	1FC/3MX/6FH	10Sim	10*	10 Sim	10*	10*	10*
52/1	*	MX	Sim	*	Sim	*	*	*

53/1	*	FC	1Não	1*	1*	1*	1*	*
54/1	NU	MX	1Sim	1Sim	1Sim	1*	1*	*
55/1	*	FC	1Sim	1Sim	1*	1*	1Sim	*
56/3	3*	3*	3*	3*	3*	3*	3*	3*
57/3	3*	2FC/1MX	3Sim	2Sim/1*	1Sim/2*	1*	3*	3*
58/1	*	MX	1Sim	1*	1Sim	1*	1*	*
Total (%)	132(24,48)NU/ 28(5,20) MOD/ 12(2,23) EU/ 367(68,09)*	220(40,82) FC/ 146(27,08) MX/ 14(2,60) FH/ 159(29,50)*	234(43,41)Não 248(46,01)Sim 57(10,58)*	116(21,52) Sim 423(78,48)*	118(21,89) Sim 421(78,11)*	28(5,20) Sim 511(94,80)*	42(7,80) Sim 497(92,20)*	2(0,37) Sim 102(18,92) Não 435(80,71)*

Legenda: NU= não ulcerado Mod= moderado, EU= extensivamente ulcerado, FC= Fibrocelular, MX= mixóide, FH= fibrohialinizado, *=Não informado

Tabela 4. Referências, número de casos, ilhas e cordões de epitélio odontogênico, quantidade, epitélio semelhante a ameloblastoma, epitélio com diferencial para células claras, células basais em brotos, imunopositividade do epitélio odontogênico de Fibromas odontogênicos periféricos.

Ref./casos	Ilhas ou cordões de ep. odontogênico	Quantidade	Ep. semelhante a ameloblastoma	Ep. com diferencial para células claras	Células basais em brotos
3/1	Não	*	*	*	*
15/10	10Sim	10*	10*	10*	10*
4/1	Sim	Abundante	1Sim	*	*
16/1	Não	*	*	*	*
17/1	Sim	Moderado	*	*	*
18/1	Não	*	*	*	*
19/1	*	*	*	*	*
20/52	7Sim/45Não	52*	52*	52*	52*
21/1	Sim	Abundante	*	*	*
5/9	9Sim	4Escasso/2Moderado/ Abundante/ 1*	9*	9*	9*
22/5	5Sim	1 Escasso/4 Moderado	5*	5*	5*
23/13	13Sim	13Abundante	13*	13*	13*
24/30	30Sim	15Escasso/9Moderado/ 4Abundante: 4 casos/2*	30*	30*	30*
7/1	Sim	Moderado	*	*	*
25/3	3Sim	3*	3*	3*	1Sim/2*
8/1	Sim	*	*		*
27/36	36Sim	36Abundante	36*	36*	36*
28/2	2Sim	2*	2Sim	2*	2*
29/1	Sim	Moderado	*	1	*
30/46	46Sim	29Escasso/11Moderado/ 6Abundante	2Sim	1Sim	37Sim
31/1	Sim	Abundante	*	*	*
32/2	2Sim	2Escasso	2*	2*	2*
33/1	Sim	*	*	*	*
34/23	23Sim	23*	23*	23*	23*
35/1	Sim	*	*	*	*
36/1	*	*	*	*	*
37/17	17Sim	11Escasso/6Moderado	17*	17*	17*
38/1	Sim	Abundante	*	*	*
39/25	25*	25*	25*	25*	25*
40/1	Sim	*	*	Sim	*
41/19	19Sim	9Escasso/6Abundante/ 4Moderado	19*	19*	19*
42/151	151Sim	151*	151*	151*	151*
43/1	Sim	*	*	*	*
59/1	Sim	*	*	*	*
44/1	Sim	Moderado	*	*	*
45/1	Sim	Abundante	*	*	*
46/40	40Sim	40*	40*	40*	40*
47/12	12Sim	12*	12*	12*	12*
48/1	Sim	*	*	*	*
49/1	*	*	*	*	*
50/1	Sim	*	*	*	*
51/10	10Sim	10*	10*	10*	10*
52/1	Sim	*	*	*	*
53/1	Sim	*	*	*	10*
54/1	Sim	Escasso	*	*	1Sim
55/1	Sim	*	*	*	*
56/3	3Sim	3*	3*	3*	3*
57/3	3Sim	2Escasso/1Abundante	3*	3*	3*
58/1	Sim	Abundante	*	*	*
Total(%)	463(85,90) Sim 48(8,90) Não 28(5,20)*	74(13,73) Abundante 39(7,24) Moderado 74(13,73)Escasso 352(65,30)*	5(0,93) Sim 534(99,07)*	3(0,55) Sim 535(99,45)*	39(7,23) Sim 500 (92,77)*

*=Não relatado

ANEXO D- Tabela 5 com as principais dificuldades encontradas no momento da extração e análise de dados por artigo.

Tabela 5- Dificuldades encontradas em cada artigo

Ref.	Dados clínicos Incompletos	Dados histopatológicos incompletos	Falta de imagens	Imagem de visualização difícil	Legendas com informações ausentes	Informações não descritas, que necessitaram ser coletadas por meio da análise da imagem	Agrupamento de dados de uma série de casos, sem individualizar cada caso
3	X	X		X		X	
15	X		X			X	X
4	X		X				
16		X	X	X		X	
17	X				X		
18	X	X		X	X	X	
19	X	X		X			
20	X	X	X				X
21	X	X	X			X	
5	X		X				
22	X		X				X
23	X	X	X	X	X		X
24	X	X	X				X
7							
25	X			X		X	
8	X		X			X	
27	X	X	X				X
28	X		X				
29	X		X				
30	X	X	X				X
31						X	
32	X		X				
33	X			X		X	
34	X	X	X				
35		X	X			X	
36		X					
37							X
38							
39	X	X	X				X
40	X	X				X	
41	X	X	X				X
42	X	X	X				X
43						X	
59							
44	X			X		X	
45				X		X	
46	X	X	X				X
47	X	X					X
48						X	
49	X			X		X	
50					X	X	
51	X	X	X				X
52						X	
53	X	X				X	
54	X	X		X	X	X	X
55	X	X		X		X	
56	X	X	X				X
57	X		X			X	
58	X			X		X	

Total (%)	36 (73,46)	23 (46,93)	24 (48,97)	13 (26,53)	5 (10,20)	23 (46,93)	16 (32,65)

ANEXO E- Participações em produções bibliográficas e eventos científicos durante o período do mestrado.

Artigos Publicados

- Schmidt MJ, **Tschoeke A**, Noronha L, Moraes RS, Mesquita RA, Grégio AM, Alanis LR, Ignácio SA, Santos JN, Lima AA, Luiz TS, Michels AC, Aguiar MC, Johann AC. Histochemical analysis of collagen fibers in giant cell fibroma and inflammatory fibrous hyperplasia. Acta Histochem. 2016 Jun;118(5):451-5.

- de Oliveira HC, **Tschoeke A**, da Cruz GC, Noronha L, de Moraes RS, Mesquita RA, de Aguiar MC, Caldeira PC, de Oliveira Ribas M, Grégio AM, Alanis LR, Ignácio SA, Dos Santos JN, de Lima AA, Johann AC. MMP-1 and MMP-8 expression in giant-cell fibroma and inflammatory fibrous hyperplasia. Pathol Res Pract. 2016 Dec;212(12):1108-1112.

Apresentação de trabalhos em congressos

- Apresentação de painel com o tema: Fibroma Odontogênico Periférico- Relato de Caso Clínico (2016, 34º Congresso Internacional de Odontologia de São Paulo);
- Apresentação oral com o tema Fibroma Odontogênico Periférico- Relato de Caso Clínico e apresentação de painel com o tema Paracoccidioidomicose- Relato de Caso Clínico Enfatizando a Importância do Cirurgião-Dentista no Diagnóstico (1º Encontro de Estomatologia e Patologia Oral do Interior do Paraná).
- Apresentação de painel com o tema Fibroma Odontogênico Periférico- Relato de Caso Clínico no VII Congresso Sul Brasileiro de Câncer Bucal e VI Jornada de Cirurgia e Traumatologia Bucomaxilofacial do Hospital Erasto Gaertner", Curitiba (2016).
- Apresentação de painel com o tema Avaliação da imunoexpressão da mmp1em fibromas de células gigantes, hiperplasias fibrosas inflamatórias na 33ª Reunião Anual da Sociedade Brasileira de Pesquisa Odontológica (SBPQO), Campinas (2016)

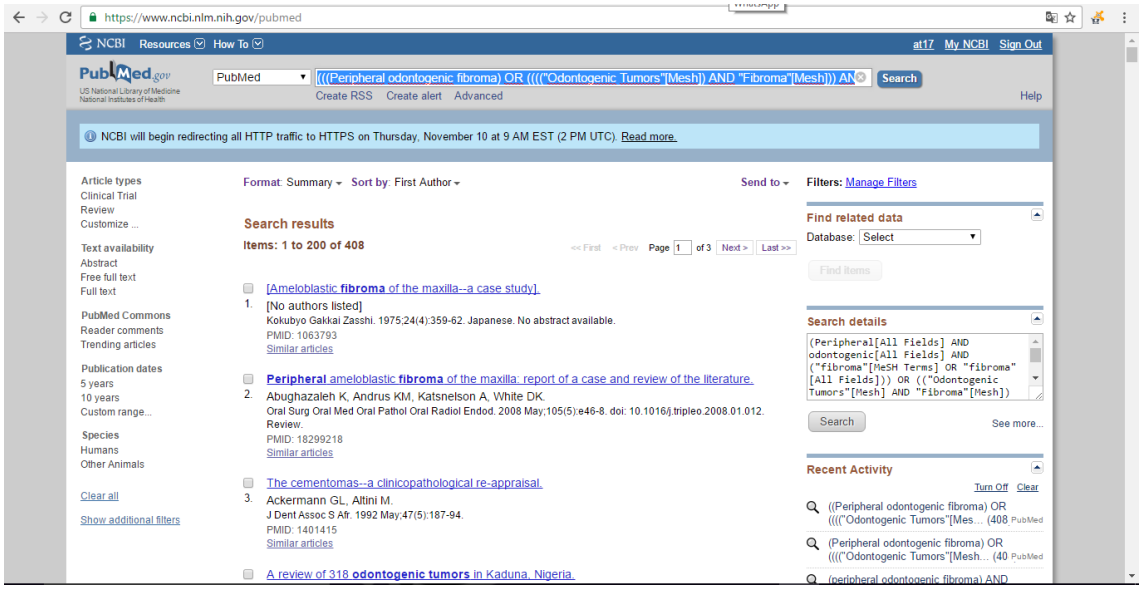
Participações em congressos

- Participação VI Congresso de Humanização realizado na PUCPR (2015);
- Participação Seminário de Emergências Médicas em Consultórios Odontológicos em Rio Negro-PR promovido pelo CRO-PR (2015, 18 horas);
- Participação 34º Congresso Internacional de Odontologia de São Paulo (2016);
- Curso sobre Manejo clínico-cirúrgico de lesões bucais frequentes na clínica odontológica (2016, 2 horas, curso dentro do 34º Congresso Internacional de Odontologia de São Paulo);

- Participação no 1º Encontro de Estomatologia e Patologia Oral do Interior do Paraná (2016, 16 horas);
- Participação no VII Congresso Sul Brasileiro de Câncer Bucal e VI Jornada de Cirurgia e Traumatologia Bucomaxilofacial do Hospital Erasto Gaertner", Curitiba (2016).
- Participação na 33ª Reunião Anual da Sociedade Brasileira de Pesquisa Odontológica (SBPQO), Campinas, (2016).

ANEXO F- Termos utilizados na busca nas bases de dados.

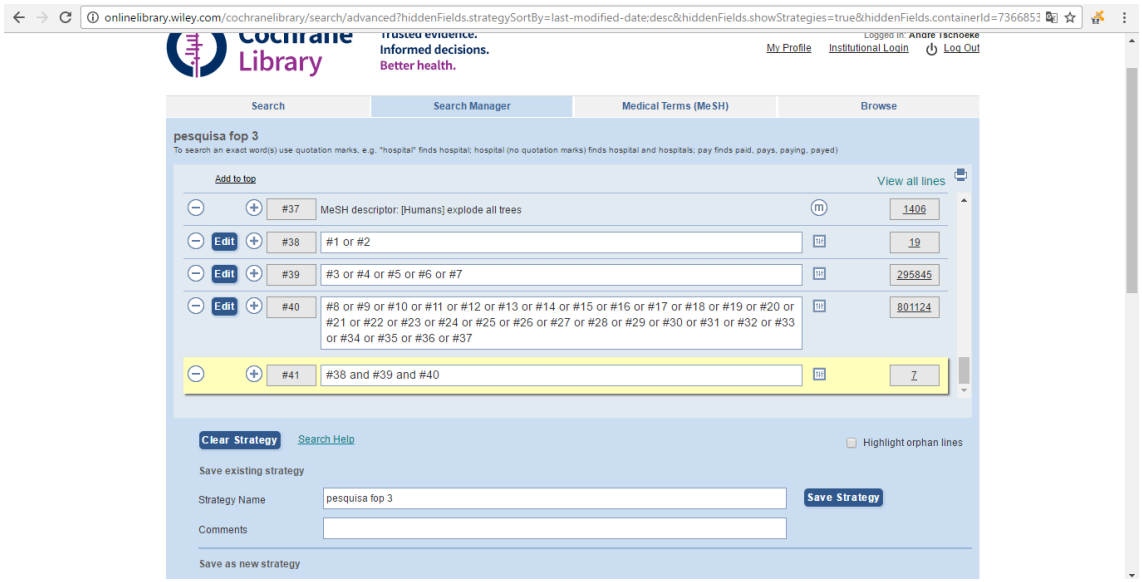
PUBMED : (((Peripheral odontogenic fibroma) OR ((((("Odontogenic Tumors"[Mesh]) AND "Fibroma"[Mesh])) AND ((((("Diagnosis"[Mesh]) OR odontogenic epithelium[Title/Abstract]) OR (nets[Title/Abstract] OR islands[Title/Abstract]) OR histopathology)) AND ((((((((("Gender Identity"[Mesh]) OR "Sex"[Mesh]) OR male[Title/Abstract]) OR female[Title/Abstract]) OR man[Title/Abstract]) OR woman[Title/Abstract])) OR (((((("Age of Onset"[Mesh]) OR years[Title/Abstract]) OR Onset Age[Title/Abstract]) OR Age-at-Onset[Title/Abstract]) OR Age at Onset[Title/Abstract])) OR (((((((("Disease Attributes"[Mesh]) OR clinical characteristics[Title/Abstract]) OR Attribute, Disease[Title/Abstract]) OR Attributes, Disease[Title/Abstract]) OR Disease Attribute[Title/Abstract]) OR nodule[Title/Abstract]) OR sessile[Title/Abstract]) OR pedicellate[Title/Abstract]) OR gingival mass[Title/Abstract])))) OR "Humans"[Mesh])))))



BIREME : (tw:(Peripheral odontogenic fibroma)) AND (tw:(tw:((tw:((tw:(odontogenic tumors)) OR (tw:(fibroma)))) AND (tw:((tw:(diagnosis)) OR (tw:(odontogenic epithelium)) OR (tw:(nets)) OR (tw:(islands)) OR (tw:(histopathology)))) AND (tw:((tw:(therapeutics)) OR (tw:(management)) OR (tw:(treatment)) OR (tw:(therapeutic)) OR (tw:(therapy)) OR (tw:(therapies)) OR (tw:(treatments)) OR (tw:(disease managements)) OR (tw:(disease management)) OR (tw:(managements, disease)) OR (tw:(case management)) OR (tw:(gender identity))

OR (tw:(sex)) OR (tw:(male)) OR (tw:(female)) OR (tw:(man)) OR (tw:(woman)) OR (tw:(age of onset)) OR (tw:(years)) OR (tw:(onset age)) OR (tw:(age-at-onset)) OR (tw:(age at onset)) OR (tw:(disease attributes)) OR (tw:(clinical characteristics)) OR (tw:(attribute, disease)) OR (tw:(attributes, disease)) OR (tw:(disease attribute)) OR (tw:(nodule)) OR (tw:(sessile)) OR (tw:(pedicullate)) OR (tw:(gingival mass)) OR (tw:(humans))))) AND (instance:"regional")))

COCHRANE



MeSH descriptor: [Odontogenic Tumors] explode all trees 11

#2 MeSH descriptor: [Fibroma] explode all trees 8

#3 MeSH descriptor: [Diagnosis] explode all trees 292559

#4 odontogenic epithelium 1

#5 Nets 1112

#6 Islands 645

#7 histopathology 2525

#8 therapeutics 18029

#9 management 73477

#10 treatment 452342

#11 therapeutic 239392

#12 MeSH descriptor: [Therapeutics] explode all trees 273313

#13 treatments 53273

#14 disease managements 64

#15 disease management 29149

#16 managements, disease 64

#17 case management 12871

#18 MeSH descriptor: [Gender Identity] explode all trees 243

#19 sex 33916

#20 male 473053

#21 female 493189

#22 man 10233

#23 woman 5898

#24 MeSH descriptor: [Age of Onset] explode all trees 595

#25 years 173104

#26 onset age 9829

#27 age-at-onset 386

#28 MeSH descriptor: [Disease Attributes] explode all trees 42574

#29 clinical characteristics 41693

#30 attribute, disease 289

#31 attributes, disease 315

#32 disease attribute 289

#33 nodule 819

#34 sessile 107

#35 pedicullate 0

#36 gingival mass 57

#37 MeSH descriptor: [Humans] explode all trees 1406

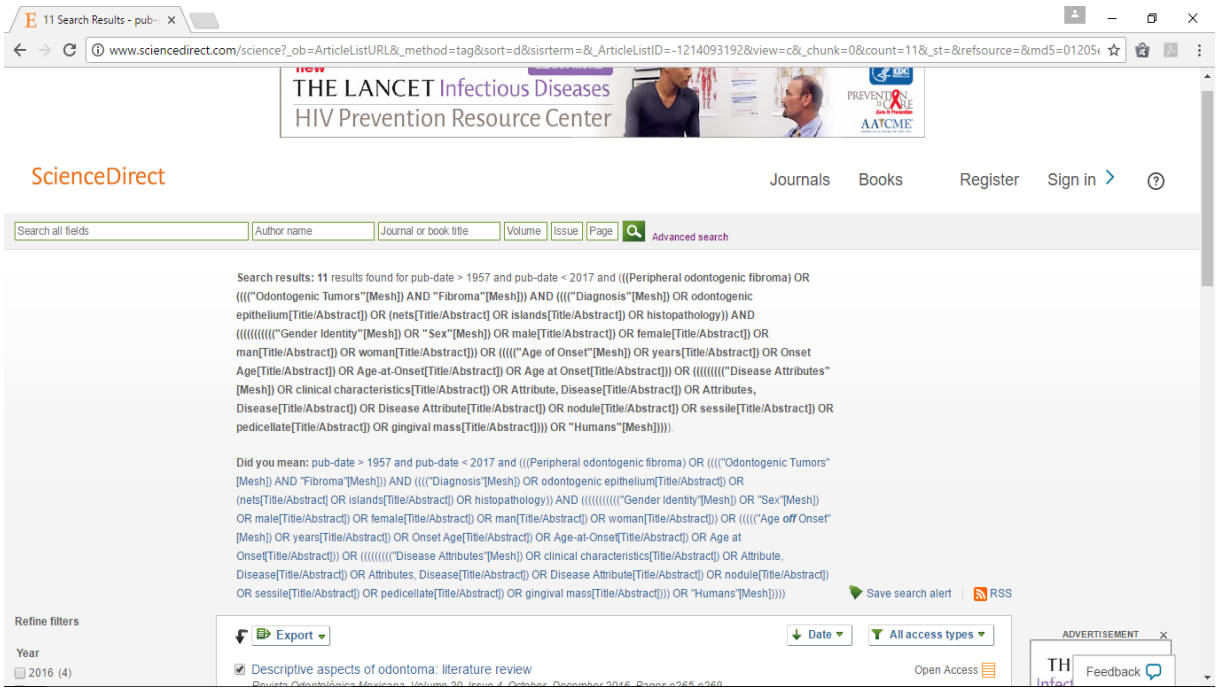
#38 #1 or #2 19

#39 #3 or #4 or #5 or #6 or #7 295832

#40 #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 801121

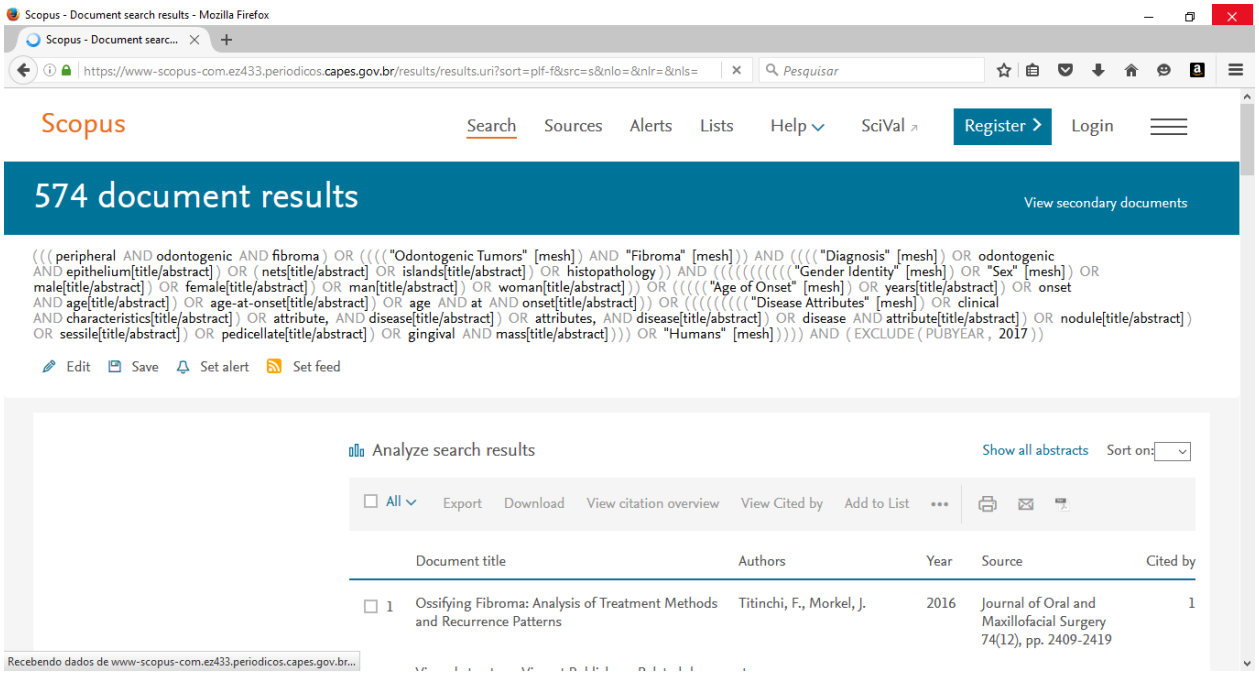
#41 #38 and #39 and #40 7

SCIENCE DIRECT: (((Peripheral odontogenic fibroma) OR ((((("Odontogenic Tumors"[Mesh]) AND "Fibroma"[Mesh])) AND ((((("Diagnosis"[Mesh]) OR odontogenic epithelium[Title/Abstract]) OR (nets[Title/Abstract] OR islands[Title/Abstract]) OR histopathology)) AND ((((((((((("Gender Identity"[Mesh]) OR "Sex"[Mesh]) OR male[Title/Abstract]) OR female[Title/Abstract]) OR man[Title/Abstract]) OR woman[Title/Abstract])) OR (((((("Age of Onset"[Mesh]) OR years[Title/Abstract]) OR Onset Age[Title/Abstract]) OR Age-at-Onset[Title/Abstract]) OR Age at Onset[Title/Abstract])) OR (((((((("Disease Attributes"[Mesh]) OR clinical characteristics[Title/Abstract]) OR Attribute, Disease[Title/Abstract]) OR Attributes, Disease[Title/Abstract]) OR Disease Attribute[Title/Abstract]) OR nodule[Title/Abstract]) OR sessile[Title/Abstract]) OR pedicellate[Title/Abstract]) OR gingival mass[Title/Abstract])))) OR "Humans"[Mesh])))))



SCOPUS

(((Peripheral odontogenic fibroma) OR ((((("Odontogenic Tumors"[Mesh]) AND "Fibroma"[Mesh])) AND ((((("Diagnosis"[Mesh]) OR odontogenic epithelium[Title/Abstract]) OR (nets[Title/Abstract] OR islands[Title/Abstract]) OR histopathology)) AND ((((((((((("Gender Identity"[Mesh]) OR "Sex"[Mesh]) OR male[Title/Abstract]) OR female[Title/Abstract]) OR man[Title/Abstract]) OR woman[Title/Abstract])) OR (((((("Age of Onset"[Mesh]) OR years[Title/Abstract]) OR Onset Age[Title/Abstract]) OR Age-at-Onset[Title/Abstract]) OR Age at Onset[Title/Abstract])) OR (((((((("Disease Attributes"[Mesh]) OR clinical characteristics[Title/Abstract]) OR Attribute, Disease[Title/Abstract]) OR Attributes, Disease[Title/Abstract]) OR Disease Attribute[Title/Abstract]) OR nodule[Title/Abstract]) OR sessile[Title/Abstract]) OR pedicellate[Title/Abstract]) OR gingival mass[Title/Abstract]))) OR "Humans"[Mesh])))))



ANEXO G- Normas para publicação

Journal of Periodontology Author Instructions *Updated April 2015*

This update includes a general reorganization of the author guidelines as well as improved navigation. Other changes include onlineonly publication, conflict of interest form collection, and updates to clinical trial registration requirements.

The *Journal of Periodontology* publishes articles relevant to the science and practice of periodontics and related areas. Manuscripts are accepted for consideration with the understanding that text, figures, photographs, and tables have not appeared in any other publication, except as an abstract prepared and published in conjunction with a presentation by the author(s) at a scientific meeting, and that material has been submitted only to this journal.

The *Journal of Periodontology* accepts manuscript submissions online at ScholarOne Manuscripts. To start a new submission, enter the Author Center and click "Click here to submit a new manuscript." Details regarding each submission step are located at the top of the page in ScholarOne Manuscripts. Authors should prepare manuscripts in accordance with the instructions below. Failure to do so may result in delays or manuscript unsubmission.

MANUSCRIPT CATEGORIES AND SPECIFIC FORMATS

Submissions to the *Journal of Periodontology* should be limited to one of the categories defined below. Specific information regarding length and format is provided for each category. Please also refer to the instructions provided under General Format and Style. All manuscripts will be reviewed by the Editors for novelty, potential to extend knowledge, and relevance to clinicians and researchers in the field. Some manuscripts will be returned without review, based on the Editors' judgment of the appropriateness of the manuscript for the *Journal of Periodontology*.

ORIGINAL ARTICLES

These are papers that report significant clinical or basic research on the pathogenesis, diagnosis, and treatment of the different forms of periodontal disease. Papers dealing with design, testing, and other features of dental implants are also included.

Format

Original articles must be limited to 4,000 words (excluding the abstract, references, and figure legends). The reference list should not exceed 50 references, and the total combined number of figures and tables must be six or fewer. Multipanel figures are acceptable.

Abstract

All original articles should be submitted with a structured abstract, consisting of no more than 250 words and the following four paragraphs:

Background: Describes the problem being addressed.

Methods: Describes how the study was performed.

Manuscript Categories
Original Articles
Review Articles

Results: Describes the primary results.
Conclusion(s): Reports what authors have concluded from these results, and notes their clinical implications.

Introduction

The Introduction contains a concise review of the subject area and the rationale for the study. More detailed comparisons to previous work and conclusions of the study should appear in the Discussion section.

Materials and Methods

This section lists the methods used in the study in sufficient detail so that other investigators would be able to reproduce the research. When established methods are used, the author need only refer to previously published reports; however, the authors should provide brief descriptions of methods that are not well known or that have been modified. Identify all drugs and chemicals used, including both generic and, if necessary, proprietary names and doses. The populations for research involving humans should be clearly defined and enrollment dates provided.

Results

Results should be presented in a logical sequence with reference to tables, figures, and supplemental material as appropriate.

Discussion

New and possible important findings of the study should be emphasized, as well as any conclusions that can be drawn. The Discussion should compare the present data to previous findings. Limitations of the experimental methods should be indicated, as should implications for future research. New hypotheses and clinical recommendations are appropriate and should be clearly identified. Recommendations, particularly clinical ones, may be included when

appropriate.
Publication of Accepted Original Articles
Please note that accepted manuscripts which are classified by the Editors as "Discovery Science" will be placed on an accelerated schedule for onlineonly
publication. See OnlineOnly
Publication
below.
REVIEW ARTICLES
These are focused reviews of basic and clinical science related to periodontics and implant dentistry. These reviews should be concise and address an important and timely clinical question. Authors should discuss clinical relevance and the impact on future understanding and practice. The review should be based on a critical assessment of the literature and should use the format and methods of a "systematic review." Detailed descriptions of the systematic review methodology are available in the Cochrane Handbook for Systematic Reviews of Interventions.1 There are many excellent published examples of systematic reviews, including "Periodontal Disease and Coronary Heart Disease Incidence: A Systematic Review and MetaAnalysis" by
Humphrey et al.2
Authors of systematic reviews that include a metaanalysis should refer to the QUOROM statement.3 Authors of systematic reviews without metaanalysis
should refer to the papers by Cook et al.4 and Mulrow et al.5
1. Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions* [serial on the Internet]. September 2008; version 5.0.1. Available at: www.cochranehandbook.org.
2. Humphrey L, Fu R, Buckley D, Freeman M, Helfand M. Periodontal disease and coronary heart disease incidence: A

systematic review and metaanalysis.
J Gen Intern Med
2008;23:20792086.
3. Moher D, Cook D, Eastwood S, Olkin I, Rennie D, Stroup D. Improving the quality of reports of metaanalyses
of
randomized controlled trials: The QUOROM statement. *Lancet* 1999;354:18961900.
4. Cook D, Mulrow C, Haynes R. Systematic reviews: Synthesis of best evidence for clinical decisions. *Ann Intern Med* 1997;126:376380.
5. Mulrow C, Langhorne P, Grimshaw J. Integrating heterogeneous pieces of evidence in systematic reviews. *Ann Intern Med* 1997;127:989995.
Format
The abstract should summarize the main conclusions of the review in 350 words or less. Systematic review articles should: define a clear and clinically relevant research question; retrieve and describe the limitations of previously published reviews on this topic; and justify the need for a systematic review. The review should then define the search strategy used to identify primary articles; describe the methods used to select primary studies; specify inclusion and exclusion criteria (criteria for selecting primary studies should be based on population studied, intervention or exposure, study

outcomes, and study methodology); perform a blinded assessment of the quality of the selected articles; describe the reliability of this process in terms of agreement between two evaluators; account for all studies identified by the search and justify exclusions; state their conclusions; compare their conclusions to the literature and current standard of care; outline the limitations of the review; and suggest areas for future research.

Papers should be balanced, literaturebased reviews that are concise (2,000 to 3,000 words) with about 100 key references. Tables and figures should be limited to those essential to convey the results of the review, and the total combined number of figures and tables should not exceed six. Since critical reviews require selection of reports and interpretation of data, authors should disclose financial interest in the companies making products or providing services described in the review.

COMMENTARIES

The purpose of these papers is to provide a forum for discussion of controversies and other issues as they relate to the practice of periodontics and implant dentistry. Full and balanced discussion of controversies on important issues is encouraged. This may result in several authors each presenting a relevant viewpoint. Commentaries should be concise (2,000 to 3,000 words) with no more than 50 references; however, they should be complete and balanced, which may require that the issue or controversy addressed be highly focused.

Introduction

This section should clearly state the clinical question or issues to be discussed and document their importance and timeliness.

Body

The body should present the information supporting all aspects of the issues. This portion of the Commentary may be subdivided as appropriate with headings. Figures, tables, and other illustrative materials may be incorporated. The total combined number of figures and tables should not exceed six.

Summary

The summary should place the issue in perspective and point a way for future directions in addressing the controversy.

Acknowledgment(s)

Since these papers allow authors to express their opinions on a

subject, it is extremely important that authors disclose any and all affiliations, financial position, or any other information that constitutes a real or perceived conflict of interest.

CASE SERIES

The *Journal of Periodontology* no longer publishes Case Reports. Authors are encouraged to submit Case Reports to *Clinical Advances in Periodontics*. The *Journal of Periodontology* publishes selected Case Series that describe unusual case presentations, complex diagnoses, and novel approaches to treatment within the scope of practice of periodontology. These Case Series provide valuable information for clinicians and teachers in the field.

Case Series report a sufficient number of consecutive or randomized cases to make a persuasive argument for or against the procedure, technique, or concept under discussion. Cases should be relatively homogeneous so that a systematic evaluation of one type of disease, lesion, or condition is made for the procedure under

consideration. Also, treatment and documentation should be consistent and standardized for all cases. It is recognized that definitive evidence for the safety and efficacy of any procedure, drug, or device comes primarily from welldesigned, randomized, controlled trials. However, wellexecuted Case Series may lead to hypotheses about the usefulness of new and innovative procedures, drugs, or devices and may therefore be of value to the progress of clinical science.

The requirements for patient consent, privacy, and institutional approval are well defined for manuscripts describing research on human subjects. These basic requirements are described by the International Committee of Medical Journal Editors (ICMJE) in their Uniform Requirements for Manuscripts Submitted to Biomedical Journals (available at: www.icmje.org) and are interpreted in the instructions to authors of all peerreviewed biomedical journals, including the *Journal of Periodontology*.

Due to the changing ethical and legal environment around the use of patient information, the editorial team has received multiple questions about the need for subject consent from patients described in Case Series submitted for publication.

The following applies to most Case Series. It should be noted that the Editors will determine whether specific Case Series require additional approvals beyond what is described below.

Requirement for Ethics Board Approval

Most Case Series are a retrospective description of clinical findings in cases or an observed course of events that document a new aspect of patient management during the normal course of clinical treatment. Since there is no hypothesis testing, no systematic data collection beyond that which is part of routine clinical practice, no data analysis, and the work has already been done, Case Series do not usually qualify as "research" requiring approval from ethical boards designed to protect humans involved in clinical research. (U.S. Fed. definition: "RESEARCH is any systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.")

Example 1: Series of private practice implant cases in patients who have been taking bisphosphonates. Authors describe the findings in each case, which are collected and reported in a table format.

Example 2: Authors collect series of private practice implant cases in patients who have or have not been taking bisphosphonates. The sample size is sufficient for data analysis, and authors analyze and report the incidence of complications.

Example 1 does not qualify as "research," but example 2 does qualify and requires ethical approval.

Please see "Does My Case Series Need IRB Approval?" for more information.

Privacy in Case Series

No patient identifiers should be included in Case Series. If the authors choose to include any subject identifiers, the authors must include the patient's informed written consent to publish the information.

Our policy conforms to the Uniform Requirements, which states: "Patients have a right to privacy that should not be violated without informed consent. Identifying information, including names, initials,

or hospital numbers, should not be published in written descriptions, photographs, or pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives written informed consent for publication. Informed consent for this purpose requires that an identifiable patient be shown the manuscript to be published. Authors should disclose to these patients whether any potential identifiable material might be available via the Internet as well as in print after publication."
It should be noted that patients may have given a signed "consent to treat," but that does not constitute permission to publish their case with personal identifiers unless they have explicitly approved the manuscript. Likewise, patient consent under government privacy rules, such as the Health Insurance Portability and Accountability Act (HIPAA) in the United States, does not constitute permission to publish their case with personal identifiers unless they have explicitly approved the manuscript.

Format

Case Series must be limited to 2,000 to 3,000 words (excluding the abstract, references, and figure legends). The reference list should not exceed 50 references, and the total combined number of figures and tables must be six or fewer. Multipanel figures are acceptable.

Abstract

Case Series should be submitted with a structured abstract, consisting of no more than 250 words and the following four paragraphs:
Background: Describes the clinical situation being discussed.
Methods: Describes the clinical procedures (surgical and nonsurgical) performed.
Results: Describes the clinical results.
Conclusion(s): Reports what authors have concluded, specifically clinical implications in practice situations.

Introduction

This section should include a critical review of the pertinent literature.

Case Description and Results

This section describes the cases, including all relevant data. For ease of presentation, tables describing longitudinal data in a chronological form may be useful. Carefully selected, highquality clinical photographs in full color, as well as radiographs, are encouraged.

Discussion

This should include findings, put into perspective with respect to the field and literature. Unique arguments and new information gained should be summarized. Consideration of the clinical significance of the cases should be emphasized in all sections.

GUEST EDITORIALS

Guest Editorials may be invited or may be submitted from authorities in certain areas as a means of offering their perspective on one or more articles published in the *Journal*, or on other items of interest to the readership.

LETTERS TO THE EDITOR

Letters may comment on articles published in the *Journal* and should offer constructive criticism. If a letter comments on a published article, the author(s) will be provided 30 days to respond to the observations.
Letters to the Editor may also address any aspect of the

profession, including education and training, new modes of practice, and concepts of disease and its management.
Letters should be brief (<1,000 words), focused on one or a few specific points or concerns, and can be signed by no more than five individuals.
Citations should be handled as standard references.

GENERAL FORMAT

Manuscripts must be submitted in Microsoft Word. Margins should be at least 1" on both sides and top and bottom and all text should be doublespaced.
Materials should appear in the following order:
Title Page
Abstract (or Introduction) and Key Words
Text
Footnotes
Acknowledgment(s)
References
Figure Legends
Tables
Figures should not be embedded in the manuscript. Please see the *Journal of Periodontology* Digital Art Guidelines for more information on submitting figures.
Authors should retain a copy of their manuscript for their own records.

TITLE PAGE

The title page should contain:
1. a concise but informative title;
2. first name, middle initial, and last name of each author, with the highest academic degree and the current institutional affiliation, including department, for each (please use footnote symbols in the sequence *, †, ‡, §, ‖, ¶, #, **, etc. to identify authors and their corresponding institutions);
3. disclaimers, if any;
4. the name and address (including fax number and email) of the author responsible for correspondence (please indicate whether fax number and email can be published);
5. word count and number of figures, tables, and references in the manuscript;
6. a short running title of no more than 60 characters, including spaces;
7. a onesentence summary describing the key finding(s) from the study.

KEY WORDS

A maximum of six key words or short phrases, drawn from MeSH documentation, to facilitate indexing should be listed below the abstract.

ACKNOWLEDGMENT(S) AND CONFLICTS OF INTEREST

Acknowledgment(s)
Following the Discussion, acknowledgments may be made to individuals who contributed to the research or the manuscript preparation at a level that did not qualify for authorship. This may include technical help or participation in a clinical study. Authors are responsible for obtaining written permission from persons listed by

name. Acknowledgments must also include a statement that includes the source of any funding for the study, and defines the commercial relationships of each author.

Conflicts of Interest

In the interest of transparency and to allow readers to form their own assessment of potential biases that may have influenced the results of research studies, the *Journal of Periodontology* requires that all authors declare potential competing interests relating to papers accepted for publication. Conflicts of interest are defined as those influences that may potentially undermine the objectivity or integrity of the research, or create a perceived conflict of interest. Authors are required to submit:

1. A statement in the acknowledgments section of the manuscript that includes the source of any funding for the study, and defines the commercial relationships of each author. If an author has no commercial relationships to declare, a statement to that effect should be included. This statement should include financial relationships that may pose a conflict of interest or potential conflict of interest. These may include financial support for research (salaries, equipment, supplies, travel reimbursement); employment or anticipated employment by any organization that may gain or lose financially through publication of the paper; and personal financial interests such as shares in or ownership of companies affected by publication of the research, patents or patent applications whose value may be affected by this publication, and consulting fees or royalties from organizations which may profit or lose as a result of publication. An example is shown below.
2. A conflict of interest and financial disclosure form for each author. A link to this electronic form will be emailed to each author after manuscript submission.

Conflict of interest information will not be used as a basis for suitability of the manuscript for publication.

Example of Conflict of Interest Statement

This study was supported by a grant from the Acme Implant Corporation, Seoul, Korea. Dr. Lee is on the scientific advisory board for Acme Implant Corporation and gives lectures sponsored by the company. Dr. Smith is a consultant and shareholder of the Brownstone Implant Corporation, Boston, Massachusetts. Dr. Wang is employed fulltime as chief technical officer of the Acme Implant Corporation. Drs. Able, Kim, and Bruce report no conflicts of interest related to this study.

REFERENCES

References should be numbered consecutively in the order in which they appear in the text. A journal, magazine, or newspaper article should be given only one number; a book should be given a different number each time it is mentioned, if different page numbers are cited.

All references are identified, whether they appear in the text, tables, or legends, by Arabic numbers in superscript. Journal title abbreviations should be those used by the U.S. National Library of Medicine. If you are uncertain about the correct abbreviation for a journal title, please search for the journal at http://www.ncbi.nlm.nih.gov/nlmcatalog.

The use of abstracts as references is strongly discouraged. Manuscripts accepted for publication may be cited and should include the manuscript's DOI, if known. Material submitted, but not yet accepted, should be cited in text as "unpublished observations."

Written and oral personal communications may be referred to in text, but not cited as references. Please provide the date of the communication and indicate whether it was in a written or oral form. In addition, please identify the individual and his/her affiliation. Authors should obtain written permission and confirmation of accuracy from the source of a personal communication. Presented papers, unless they are subsequently published in a proceedings or peerreviewed journal, may not be cited as references. In addition, Wikipedia.org may not be cited as a reference. For most manuscripts, authors should limit references to materials published in peerreviewed professional journals. In addition, authors should verify all references against the original documents. References should be typed doublespaced.

Examples of references are given below. Authors are encouraged to consult EndNote for the *Journal of Periodontology*'s preferred reference style.

Journals

1. Standard journal reference. Note: list all authors if six or fewer; when seven or more, list only first three and add et al. KuritaOchiai T, Seto S, Suzuki N, et al. Butyric acid induces apoptosis in inflamed fibroblasts. *J Dent Res* 2008;87:5155.
2. Corporate author. Federation Dentaire Internationale. Technical report no. 28. Guidelines for antibiotic prophylaxis of infective endocarditis for dental patients with cardiovascular disease. *Int Dent J* 1987;37:235.
3. Journal paginated by issue. Card SJ, Caffesse RG, Smith BA, Nasjleti CE. New attachment following the use of a resorbable membrane in the treatment of periodontitis in dogs. *Int J Periodontics Restorative Dent* 1989;9(1):5969.
4. Non–Englishlanguage titles translated into English. Buchmann R, Khoury F, Hesse T, Müller RF, Lange DE. Antimicrobial therapy of periimplant disease (in German). *Z Zahnärztl Implantol* 1996;12:152157.

Books and Other Monographs

5. Personal author(s). Tullman JJ, Redding SW. *Systemic Disease in Dental Treatment*. St. Louis: The CV Mosby Company; 1983:15.
6. Chapter in a book. Rees TD. Dental management of the medically compromised patient. In: McDonald RE, Hurt WC, Gilmore HW, Middleton RA, eds. *Current Therapy in Dentistry*, vol. 7. St. Louis: The CV Mosby Company; 1980:37.
7. Agency publication. Miller AJ, Brunelle JA, Carlos JP, Brown LJ, Loë H. Oral Health of United States Adults. Bethesda, MD: National Institute of Dental Research; 1987. NIH publication no. 872868.
8. Dissertation or thesis. Teerakapong A. Langerhans' cells in human periodontally healthy and diseased gingiva. [Thesis]. Houston, TX: University of Texas; 1987. 92 p.

Electronic Citations

Note: DOIs are preferred for journal articles. If a DOI is not available, please provide a URL and access date.

9. Onlineonly

article. Rasperini G, Acunzo R, Limiroli E. Decision making in gingival recession treatment: Scientific evidence and clinical experience. *Clin Adv Periodontics* 2011;1:4152. doi:10.1902/cap.2011.100002.
10. Ahead of print. McGuire MK, Scheyer ET, Nevins M, et al. Living cellular construct for increasing the width of keratinized gingiva. Results from a randomized, withinpatient, controlled trial [published online ahead of print March 29, 2011]. *J Periodontol*; doi:10.1902/jop.2011.100671.
11. Web sites. Centers for Disease Control and Prevention. Periodontal Disease. Available at: http://www.cdc.gov/OralHealth/topics/periodontal_disease.htm. Accessed September 29, 2010.

TABLES

Tables should be numbered consecutively in Arabic numbers in the order of their appearance in the text. A brief descriptive title should be supplied for each. Explanations, including abbreviations, should be listed as footnotes, not in the heading. Every column should have a heading. Statistical measures of variations such as standard deviation or standard error of the mean should be included as appropriate in the footnotes. Do not use internal horizontal or vertical rules. The submission system will easily read tables created with Word's table utility or when inserted into Word from Excel.

FIGURES

Please see the *Journal of Periodontology* Digital Art Guidelines for detailed instructions on submitting highquality images.

Figure Legends

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