



**UNIVERSIDADE FEDERAL FLUMINENSE
FACULDADE DE ODONTOLOGIA**

**PROGNÓSTICO EM LONGO PRAZO DOS AUTOTRANSPLANTES DENTÁRIOS –
UMA REVISÃO SISTEMÁTICA E META-ANÁLISE**

Niterói
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**PROGNÓSTICO EM LONGO PRAZO DOS AUTOTRANSPLANTES DENTÁRIOS –
UMA REVISÃO SISTEMÁTICA E META-ANÁLISE**

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Dissertação apresentada à Faculdade de Odontologia da Universidade Federal Fluminense, como parte dos requisitos para obtenção do título de Mestre, pelo Programa de Pós-Graduação em Odontologia.

Área de Concentração: Ortodontia

Orientador: Prof. Dr. Oswaldo de Vasconcellos Vilella.

Co-orientadora: Prof^a. Dr^a. Cláudia Trindade Mattos

Niterói

2015

BANCA EXAMINADORA

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Instituição: Faculdade de Odontologia da UFF

Decisão: _____ Assinatura: _____

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À funcionária D. Elisete, pela forma exemplar que executa suas tarefas e pela atenção e carinho que dedica aos alunos.

RESUMO

Machado LA. Prognóstico em longo prazo dos autotransplantes dentários – uma revisão sistemática e meta-análise [dissertação]. Niterói: Universidade Federal Fluminense, Faculdade de Odontologia; 2015.

Objetivo: Através de revisão sistemática da literatura apresentar o prognóstico de dentes autotransplantados com seis ou mais anos de pós-operatório e diferentes estágios de formação radicular no momento da cirurgia. **Material e métodos:** Uma extensa pesquisa bibliográfica foi realizada em cinco bases de dados eletrônicas: PubMed, Scopus, Web of Science, Lilacs e Cochrane Library. Critérios de inclusão e exclusão foram estabelecidos para selecionar os artigos de interesse. Os resultados avaliados foram: 1. taxa de sobrevivência; 2. percentual de dentes com mobilidade anormal; 3. condições pulpares; 4. percentual de dentes com reabsorção radicular. Dados diretamente relacionados com os resultados pesquisados foram extraídos dos artigos incluídos de forma independente por dois autores. Uma meta-análise foi realizada com parte dos dados coletados. **Resultados:** O levantamento nas bases de dados originou 1848 artigos. Todos foram analisados de acordo com os critérios de elegibilidade estabelecidos e seis estudos foram incluídos. A taxa de sobrevivência variou de 75,3% a 91% e a meta-análise forneceu uma magnitude do efeito de 81% ($p < 0,0001$). O percentual de anquilose variou de 4,2% a 18,2% com magnitude do efeito igual a 8% ($p < 0,0001$). A taxa de reabsorção radicular variou de 3 a 10% e a magnitude do efeito calculada foi de 4% ($p < 0,0001$). Não foi possível realizar meta-análise com os dados obtidos da avaliação das condições pulpares e do percentual de dentes com mobilidade. **Conclusão:** Através dos dados coletados, verificou-se que a taxa de sobrevivência foi excelente, considerando o período de observação. As taxas de anquilose e reabsorção radicular, apesar de pequenas, influenciam o prognóstico dos dentes autotransplantados.

Palavras-chave: dente; transplante autólogo; prognóstico

ABSTRACT

Machado LA. Long-term prognosis of tooth autotransplantations – a systematic review and meta-analysis [dissertation]. Niterói: Federal Fluminense University, School of Dentistry; 2015.

Aim: To evaluate, by conducting a systematic review, the prognosis of autotransplanted teeth followed for a period equal to or greater than six years, with different stages of root formation at the time of surgery. **Material and Methods:** An extensive literature search was conducted in five electronic databases: PubMed, Scopus, Web of Science, Lilacs and The Cochrane Library. Inclusion and exclusion criteria were established to select articles of interest. The evaluated outcomes were: 1. survival rate; 2. percentage of abnormal mobility; 3. pulp conditions; 4. percentage of root resorption. Data directly related to measures of the outcomes were extracted from the studies independently by two authors. A meta-analysis was performed with part of the collected data. **Results:** Searches of the electronic databases identified 1848 articles. All studies were analyzed in accordance with the eligibility criteria and six were included. The survival rate ranged from 75.3% to 91% and the meta-analysis provided an effect size of 81% ($p < 0.0001$). The ankylosis percentage ranged from 4.2% to 18.2% and the effect size provided was 8% ($p < 0.0001$). The root resorption percentage ranged from 3 to 10% and the effect size was equal to 4% ($p < 0.0001$). It was not possible to perform a meta-analysis with data obtained from the evaluation of pulp conditions and percentage of teeth with abnormal mobility. **Conclusion:** The data collected showed that the survival rate was excellent, considering the observation period. The rates of ankylosis and root resorption, despite their low values, influence the prognosis of autologous transplanted teeth.

Keywords: tooth; transplantation, autologous; prognosis

1- INTRODUÇÃO

É possível que crianças e adultos jovens apresentem ausências dentárias congênitas ou perdas por cárie ou trauma. As opções típicas para restauração são próteses parciais fixas, implantes, aparelhos removíveis¹ e fechamento do espaço ortodonticamente². Existe outra alternativa, não muito utilizada, que é o autotransplante¹, onde um dente é movido cirurgicamente de um local para outro da boca no mesmo indivíduo³.

O autotransplante dentário é um eficiente método de tratamento. Seu valor recai sobre o fato de permitir a reconstrução dentária usando o material mais biocompatível possível, o próprio dente do paciente⁴.

O autotransplante dentário pode ser realizado numa idade precoce, onde a incidência de traumatismo é maior, pode ser movimentado ortodonticamente⁵ e possui potencial para induzir o crescimento alveolar durante o processo eruptivo^{6,7}.

Durante a extração ocorre ruptura total do feixe vículo-nervoso e das fibras periodontais. Portanto, o sucesso do autotransplante depende do processo de cicatrização dos tecidos envolvidos⁴ e da ocorrência ou não de complicações.

A cicatrização pulpar geralmente restaura o conteúdo do canal, incluindo o suporte nervoso e vascular. A previsibilidade desta resposta parece estar fortemente relacionada com a dimensão do forame apical⁸. Uma cicatrização favorável do ligamento periodontal depende da quantidade de células viáveis presentes na superfície radicular. Se o dente doador é extraído com dano mínimo ao ligamento periodontal, a cicatrização provavelmente será bem sucedida⁷.

Áreas danificadas do ligamento periodontal e da superfície radicular são atacadas pelo processo de reabsorção, podendo levar à perda de cemento e dentina. A profundidade da cavidade formada pela reabsorção inicial e o estado pulpar são fatores que determinarão qual dos tipos de reabsorção se instalará em seguida, a inflamatória ou a de superfície. Se a cavidade for suficientemente profunda, a ponto de atingir a camada intermediária do cemento e contatar os túbulos dentinários que estão em comunicação com tecido pulpar necrótico e infectado, a reabsorção inflamatória irá se instalar como resultado da difusão de elementos tóxicos do canal para a cavidade formada. Entretanto, se a cavidade for rasa e não penetrar na camada intermediária de cemento, um dente que apresentar alterações pulpares similares irá desenvolver somente reabsorção de superfície

porque a camada intermediária do cimento irá impedir a difusão dos elementos tóxicos⁹.

A reabsorção inflamatória geralmente progride até a exposição do canal radicular¹⁰, enquanto que, na reabsorção de superfície, um novo espaço do ligamento periodontal é estabelecido¹¹.

Outro tipo possível de reabsorção radicular que pode ocorrer em dentes autotransplantados é a reabsorção substitutiva (anquilose)¹². Este fenômeno pode ser causado por um grande dano à superfície radicular do dente doador durante a cirurgia. Nesta condição, células programadas para formar osso irão atacar áreas da raiz. Um processo fisiológico de *turnover* ósseo se instalará, como aconteceria em qualquer parte do corpo. A raiz é reabsorvida, assim como o osso adjacente, sendo que no estágio de aposição, o osso, e não a dentina, preenche a área reabsorvida previamente⁷.

O acompanhamento dos dentes autotransplantados é comum até um ano após a cirurgia. Entretanto, para avaliar o sucesso do autotransplante dentário, é importante verificar o processo de cicatrização tecidual e sua evolução ao longo dos anos, uma vez que este procedimento é utilizado com mais frequência em crianças e adolescentes.

Ao elaborarmos essa revisão sistemática, pretendemos preencher uma lacuna existente na literatura, apresentando os resultados em longo prazo referente à mobilidade, índice de sobrevivência e condições pulpar e radicular dos dentes autotransplantados com diferentes estágios de formação da raiz no momento da cirurgia.

2 - METODOLOGIA

A presente revisão sistemática foi elaborada segundo o *Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist* e projetada com o objetivo de responder à pergunta: qual é a taxa de sobrevivência, qual é o grau de mobilidade e qual a condição pulpar e radicular de dentes autotransplantados com seis ou mais anos de pós-operatório?

Uma extensa pesquisa bibliográfica foi realizada em várias bases de dados eletrônicas: PubMed, Scopus, Web of Science, Lilacs e Cochrane Library.

A estratégia de busca foi feita seguindo a regra de sintaxe de cada base de dados e os seguintes protocolos de pesquisa foram estabelecidos:

Pubmed:	((tooth[ti] or teeth[ti]) and (transplantation, autologous[mh] OR autotransplantation[ti] OR autotransplanted[ti] OR transplantation[mh] OR transplantation[ti] OR transplanted[ti])) AND(tooth[mh] OR tooth[ti] OR teeth[ti] OR bicuspid[mh] OR premolar*[ti] OR incisor[mh] OR incisor*[ti] OR molar, third[mh] OR "third molar"[ti] OR "third molars"[ti] OR "wisdom teeth"[ti] OR "wisdom tooth"[ti] OR cuspid[mh] OR "canine teeth"[ti] OR "canine tooth"[ti] OR "maxillary canine"[ti] OR "mandibular canine" OR molar[mh] OR molar*[ti])
Scopus:	(TITLE("transplantation, autologous" OR autotransplantation OR autotransplanted OR transplantation OR transplanted)) AND (TITLE-ABS-KEY(tooth OR teeth OR bicuspid OR premolar* OR incisor* OR "molar third" OR "third molar" OR "third molars" OR "wisdom teeth" OR "wisdom tooth" OR cuspid* OR "canine teeth" OR "canine tooth" OR "maxillary canine" OR "mandibular canine" OR molar*))
Web of Science:	TI=("transplantation, autologous" OR autotransplantation OR autotransplanted OR transplantation OR transplanted)ANDTS=(tooth OR teeth OR bicuspid OR premolar* OR incisor* OR "molar, third" OR "third molar" OR "third molars" OR "wisdom teeth" OR "wisdom tooth" OR cuspid* OR "canine teeth" OR "canine tooth" OR "maxillary canine" OR "mandibular canine" OR molar*)
Lilacs:	MH: transplante autólogo OR MH: transplante OR autotransplante OR autotrasplante OR autotransplantation OR autotransplantado OR autotrasplantado OR autotransplantedOR transplante OR trasplante OR transplantation OR transplantado ORtrasplantado OR transplanted MH: dente OR MH: dente pré-molar OR MH: incisivo OR MH: terceiro molar OR MH: dente canino OR MH: molar OR dente* OR diente* OR tooth OR teeth OR pré-molar* OR premolar* OR incisivo* OR incisor* OR terceiro molar OR terceiros molares OR siso* OR tercer molar OR terceros molars OR third molar OR third molars OR wisdom teeth OR wisdom tooth OR dente canino OR dentes caninos OR diente canino OR dientes caninos OR cuspid* OR canine teeth OR canine tooth OR molar*

The Cochrane Library	<p>#1autotransplantation or autotransplanted:ti,ab,kw (Word variations have been searched)</p> <p>#2MeSH descriptor: [Transplantation, Autologous] explode all trees</p> <p>#3transplantation or transplanted:ti,ab,kw (Word variations have been searched)</p> <p>#4MeSH descriptor: [Transplantation] explode all trees</p> <p>#5Enter terms for search: #1 or #2 or #3 or #4</p> <p>#6tooth or teeth:ti,ab,kw (Word variations have been searched)</p> <p>#7MeSH descriptor: [Tooth] explode all trees</p> <p>#8premolar or premolars:ti,ab,kw (Word variations have been searched)</p> <p>#9MeSH descriptor: [Bicuspid] explode all trees</p> <p>#10incisor or incisors:ti,ab,kw (Word variations have been searched)</p> <p>#11MeSH descriptor: [Incisor] explode all trees</p> <p>#12"third molar" or "third molars" or "wisdom teeth" or "wisdom tooth":ti,ab,kw (Word variations have been searched)</p> <p>#13MeSH descriptor: [Molar, Third] explode all trees</p> <p>#14"canine teeth" or "canine tooth" or "maxillary canine" or "mandibular canine":ti,ab,kw (Word variations have been searched)</p> <p>#15MeSH descriptor: [Cuspid] explode all trees</p> <p>#16molar or molars:ti,ab,kw (Word variations have been searched)</p> <p>#17MeSH descriptor: [Molar] explode all trees</p> <p>#18Enter terms for search: #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17</p> <p>#19Enter terms for search:#5 and #18</p>
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Alguns filtros foram utilizados na estratégia de busca. No Pubmed foram utilizados filtros de data (01/01/1990 a 07/07/2014) e espécie (humanos). Nas outras quatro bases de dados apenas o filtro de data (1990 até 2014) foi utilizado.

A procura manual de referências em estudos de revisão relevantes também foi conduzida.

Os critérios de inclusão para a seleção foram: 1. Ensaio controlado ou estudos prospectivos ou retrospectivos; 2. Estudos que relatam a taxa de

sobrevivência e/ou condição da polpa e/ou mobilidade e/ou presença de anquilose e/ou reabsorção da raiz dos dentes autotransplantados com formação radicular completa e/ou incompleta; 3. Estudos em que todos os casos da amostra foram acompanhados por um período igual ou superior a seis anos.

Os critérios de exclusão foram: 1. Relatos de casos, séries de casos, artigos de opinião e artigos de revisão; 2. Estudos que relatam dentes autotransplantados em pacientes com doença sistêmica ou em pacientes com síndromes ou fissura lábio-palatina; 3. Estudos em animais; 4. Estudos de dentes criopreservados ou mantidos em meios de cultura; 5. Estudos que relatam autotransplante de dentes com história de cisto, tumor ou trauma; 6. Estudos com dentes esterilizados; 7. Estudos utilizando membrana; 8. Estudos com transplante intra-alveolar de dentes com fratura de raiz; 9. Estudos com presença de fístula buco-sinusal; 10. Estudo de autotransplante dentário associado a elevação do seio maxilar; 11. Estudos de dentes submetidos a reimplante intencional para realizar tratamento endodôntico.

Não houve restrição com relação ao idioma empregado na redação dos artigos.

Na fase inicial, os títulos e resumos dos potenciais artigos levantados na pesquisa foram analisados. Os estudos que não estavam de acordo com os critérios de elegibilidade foram excluídos. A leitura completa do texto do artigo foi realizada quando o resumo não estava disponível ou quando o resumo indicou que os critérios de elegibilidade estavam cumpridos.

Cada título e resumo foi analisado de forma independente por dois pesquisadores (LAM e RRN) e as informações obtidas foram comparadas. Conflitos inter-examinadores foram resolvidos por um dos autores (OVV) em uma reunião de consenso.

Após a seleção dos artigos que preencheram os critérios de inclusão, foi feita a avaliação da qualidade metodológica de cada um deles através do emprego do *Methodological Index for Non-Randomized Studies (MINORS)*¹³.

Os dados diretamente relacionados com as medidas e resultados de interesse foram extraídos dos artigos de forma independente por dois dos autores (LAM e CTM). Qualquer discordância, nesta fase, foi resolvida por discussão.

Os resultados avaliados foram: 1. O percentual de dentes transplantados presentes no exame em relação ao número total de dentes que foram

transplantados (taxa de sobrevivência); 2. O percentual de dentes com mobilidade anormal; 3. As condições pulpares; 4. O percentual de reabsorção radicular.

Uma meta-análise foi realizada através do *software Comprehensive Meta Analysis* (versão 3.2, EUA). Os valores relativos aos eventos e à amostra total foram coletados, nos estudos em que foram relatados, com a finalidade de determinar a magnitude do efeito combinado para a taxa de sobrevivência e de reabsorção radicular. A heterogeneidade entre os estudos foi registrada e uma análise de sensibilidade foi realizada.

3 - ARTIGO PRODUZIDO

Long-term prognosis of tooth autotransplantations – a systematic review and meta-analysis

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Keywords: tooth; transplantation, autologous; prognosis

ABSTRACT

Aim: To evaluate, by conducting a systematic review, the prognosis of autotransplanted teeth followed for a period equal to or greater than six years, with different stages of root formation at the time of surgery. **Material and Methods:** An extensive literature search was conducted in five electronic databases: PubMed, Scopus, Web of Science, Lilacs and The Cochrane Library. Inclusion and exclusion criteria were established to select articles of interest. The evaluated outcomes were: 1. survival rate; 2. percentage of abnormal mobility; 3. pulp conditions; 4. percentage of root resorption. Data directly related to measures of the outcomes were extracted from the studies independently by two authors. A meta-analysis was performed with part of the collected data. **Results:** Searches of the electronic databases identified 1848 articles. All studies were analyzed in accordance with the eligibility criteria and six were included. The survival rate ranged from 75.3% to 91% and the meta-analysis provided an effect size of 81% ($p < 0.0001$). The ankylosis percentage ranged from 4.2% to 18.2% and the effect size provided was 8% ($p < 0.0001$). The root resorption percentage ranged from 3 to 10% and the effect size was equal to 4% ($p < 0.0001$). It was not possible to perform a meta-analysis with data obtained from the evaluation of pulp conditions and percentage of teeth with abnormal mobility. **Conclusion:** The data collected showed that the survival rate was excellent, considering the observation period. The rates of ankylosis and root resorption, despite their low values, influence the prognosis of autologous transplanted teeth.

Keywords: tooth; transplantation, autologous; prognosis

INTRODUCTION

Children or young adults can have congenitally missing teeth or loss from trauma or caries. The restorative options are typically bridges, implants, removable appliances¹ and space closure². Often overlooked and misunderstood, another treatment option exists in autotransplantation¹, where a tooth is moved surgically from one site at the mouth to another in the same individual³. It is an efficient method of surgical treatment. Its value relies on the fact that it enables denture reconstruction using the most biocompatible material which is the patient's own tooth⁴.

Tooth transplantation can be performed at an early age, where the trauma incidence is at its maximum. Transplanted teeth can be moved orthodontically⁵ and retain the potential to induce alveolar bone growth during the eruption process^{6,7}.

During donor tooth extraction, a total rupture of the vasculoneural bundle and periodontal fibers occurs. The success of autotransplantations depends on tissues' healing processes after the surgery⁴.

Pulp healing is usually characterized by restoration of the content of the canal including the vascular and nervous supply. The predictability of this healing response appears to be strongly related to the dimensions of the apical foramen⁸. Favorable healing of the periodontal ligament depends on how many viable cells are preserved on the root surface. If donor teeth are extracted with minimal mechanical damage to the periodontal ligament, successful healing should be expected⁷.

Damaged periodontal ligament areas and damaged parts of the root surface are attacked by a resorption process, whereby resorption of cementum and dentin may occur. Inflammatory resorption or surface resorption will then start, depending on the pulpal status and the depth of the resorption cavity. If the resorption cavity penetrates the intermediate layer of cementum and contacts dentinal tubules that are in communication with infected necrotic pulp tissue, then inflammatory resorption will take place. However, if the resorption cavity is shallow and does not penetrate the intermediate layer of cementum, a tooth that displays similar pulpal changes will elicit only surface resorption because the intermediate layer of cementum will tend to arrest the diffusion of toxic elements⁹.

Inflammatory root resorption usually progresses until the root canal is exposed¹⁰. In surface resorption a new periodontal ligament space is established¹¹.

Another type of root resorption that can occur is the ankylosis¹². This phenomenon may be caused by large injury to the root surface of a donor tooth during surgery. In this condition, cells programmed to form bone will attack some areas of the root. The root is resorbed (like the adjacent bone) but in the apposition stage, bone, and not dentin, fills the previously resorbed area⁷.

Evaluations of autotransplanted teeth in the first year postoperation are common. However, to assess the success of tooth autotransplantations, tissues` healing processes and their evolution along the years should be checked, once this procedure is used more frequently in children and adolescents.

Until now, no systematic review accessing these outcomes in long term could be found in the literature. Therefore, by conducting the present research we attempted to evaluate in a long term period the survival rate, mobility and the pulpar and root conditions of autotransplanted teeth with different stages of root formation at the moment of the surgery.

MATERIAL AND METHODS

The report of this systematic review followed the PRISMA checklist. Its protocol was designed to answer the following question: what are the survival rate, the mobility degree and both pulp and root conditions of autotransplanted teeth at least six years postoperation?

An extensive literature search was conducted in five electronic databases: PubMed, Scopus, Web of Science, Lilacs and The Cochrane Library.

The search strategy was performed according to each database syntax rules and the search protocols established can be found in Table 1:

Table 1. Search protocol for each database:

Pubmed:	<p>((tooth[tj] or teeth[tj]) and (transplantation, autologous[mh] OR autotransplantation[tj] OR autotransplanted[tj] OR transplantation[mh] OR transplantation[tj] OR transplanted[tj])) AND(tooth[mh] OR tooth[tj] OR teeth[tj] OR bicuspid[mh] OR premolar*[tj] OR incisor[mh] OR incisor*[tj] OR molar, third[mh] OR "third molar"[tj] OR "third molars"[tj] OR "wisdom teeth"[tj] OR "wisdom tooth"[tj] OR cuspid[mh] OR "canine teeth"[tj] OR "canine tooth"[tj] OR "maxillary canine"[tj] OR "mandibular canine" OR molar[mh] OR molar*[tj])</p>
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Scopus	(TITLE("transplantation, autologous" OR autotransplantation OR autotransplanted OR transplantation OR transplanted)) AND (TITLE-ABS-KEY(tooth OR teeth OR bicuspid OR premolar* OR incisor* OR "molar third" OR "third molar" OR "third molars" OR "wisdom teeth" OR "wisdom tooth" OR cuspid* OR "canine teeth" OR "canine tooth" OR "maxillary canine" OR "mandibular canine" OR molar*))
Web of Science:	TI=("transplantation, autologous" OR autotransplantation OR autotransplanted OR transplantation OR transplanted) AND TS=(tooth OR teeth OR bicuspid OR premolar* OR incisor* OR "molar, third" OR "third molar" OR "third molars" OR "wisdom teeth" OR "wisdom tooth" OR cuspid* OR "canine teeth" OR "canine tooth" OR "maxillary canine" OR "mandibular canine" OR molar*)
Lilacs:	MH: transplante autólogo OR MH: transplante OR autotransplante OR autotrasplante OR autotransplantation OR autotransplantado OR autotrasplantado OR autotransplanted OR transplante OR trasplante OR transplantation OR transplantado OR trasplantado OR transplanted AND MH: dente OR MH: dente pré-molar OR MH: incisivo OR MH: terceiro molar OR MH: dente canino OR MH: molar OR dente* OR diente* OR tooth OR teeth OR pré-molar* OR premolar* OR incisivo* OR incisor* OR terceiro molar OR terceiros molares OR siso* OR tercer molar OR terceros molars OR third molar OR third molars OR wisdom teeth OR wisdom tooth OR dente canino OR dentes caninos OR diente canino OR dientes caninos OR cuspid* OR canine teeth OR canine tooth OR molar*
The Cochrane Library	<p>#1autotransplantation or autotransplanted:ti,ab,kw (Word variations have been searched)</p> <p>#2MeSH descriptor: [Transplantation, Autologous] explode all trees</p> <p>#3transplantation or transplanted:ti,ab,kw (Word variations have been searched)</p> <p>#4MeSH descriptor: [Transplantation] explode all trees</p> <p>#5Enter terms for search: #1 or #2 or #3 or #4</p> <p>#6tooth or teeth:ti,ab,kw (Word variations have been searched)</p> <p>#7MeSH descriptor: [Tooth] explode all trees</p> <p>#8premolar or premolars:ti,ab,kw (Word variations have been searched)</p> <p>#9MeSH descriptor: [Bicuspid] explode all trees</p> <p>#10incisor or incisors:ti,ab,kw (Word variations have been searched)</p>

	<p>#11MeSH descriptor: [Incisor] explode all trees</p> <p>#12"third molar" or "third molars" or "wisdom teeth" or "wisdom tooth":ti,ab,kw (Word variations have been searched)</p> <p>#13MeSH descriptor: [Molar, Third] explode all trees</p> <p>#14"canine teeth" or "canine tooth" or "maxillary canine" or "mandibular canine":ti,ab,kw (Word variations have been searched)</p> <p>#15MeSH descriptor: [Cuspid] explode all trees</p> <p>#16molar or molars:ti,ab,kw (Word variations have been searched)</p> <p>#17MeSH descriptor: [Molar] explode all trees</p> <p>#18Enter terms for search: #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17</p> <p>#19Enter terms for search:#5 and #18</p>
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Some filters were used in the search strategy. In Pubmed, date (1990/01/01 to 2014/07/07) and species (humans) filters were used. In the other four databases only the date (1990 to 2014) filter was used.

Manual searching of references of relevant review studies was also conducted to retrieve potential literature.

The inclusion criteria were: 1. Controlled trials or prospective or retrospective studies; 2. Studies reporting at least one of the following: survival rate, pulp condition, mobility, presence of ankylosis and root resorption of autotransplanted teeth with complete or incomplete root formation; 3. Studies in which all patients were followed for a period equal to or greater than six years.

The exclusion criteria were: 1. Case reports, series of cases, opinion articles and review articles; 2. Studies reporting autotransplanted teeth in patients with systemic disease, syndromes or cleft lip and palate; 3. Animal studies; 4. Studies of cryopreserved teeth or maintained in culture media; 5. Studies reporting autotransplantation of teeth with history of cyst, tumor or trauma; 6. Studies including sterilized teeth; 7. Studies using membrane; 8. Studies with intra-alveolar transplantation of teeth with root fracture; 9. Studies with presence of oroantral

fistula; 10. Study of tooth autotransplantation associated with maxillary sinus lifting; 11. Teeth subjected to intentional replantation to perform endodontic treatment.

No restrictions were made on language.

In the initial stage, titles and abstracts retrieved of potential articles were analyzed and studies that did not meet the eligibility criteria were excluded. A full-text analysis was performed when the abstract was unavailable or when the abstract suggested that the eligibility criteria were fulfilled.

Each title and abstract was reviewed independently by two researchers (LAM and RRN) and the information obtained was compared. Interexaminer conflicts were solved by another author (OVV) in a consensus meeting.

Articles that fulfilled the eligibility criteria were methodologically assessed for quality according to the Methodological Index for Non-Randomized Studies (MINORS)¹³.

Data directly related to measures of the outcomes of interest were registered and extracted independently and in duplicate by two authors (LAM and CTM). Any disagreement between reviewers at this stage was solved by discussion.

The evaluated outcomes were: 1. Percentage of transplanted teeth that were still present at the examination relative to the total number of teeth that were transplanted (survival rate); 2. Percentage of abnormal mobility; 3. Pulp conditions; 4. Percentage of root resorption.

A meta-analysis was performed using the Comprehensive Meta Analysis software (version 3.2, USA). Events and total sample were collected from each study where they were reported in order to achieve a combined effect size for the survival rate and root resorption. Heterogeneity among studies was recorded and a sensitivity analysis was performed.

RESULTS

Searches of the electronic databases identified 1848 titles and abstracts which were entered into a flow diagram (Figure 1). Among these titles, 297 were duplicated and, therefore, removed. All remaining titles and abstracts (1551) were analyzed, and 1490 were considered inappropriate and, subsequently, excluded. The full texts of 61

studies were assessed. Finally, 6 articles that fully fit the inclusion criteria were selected.

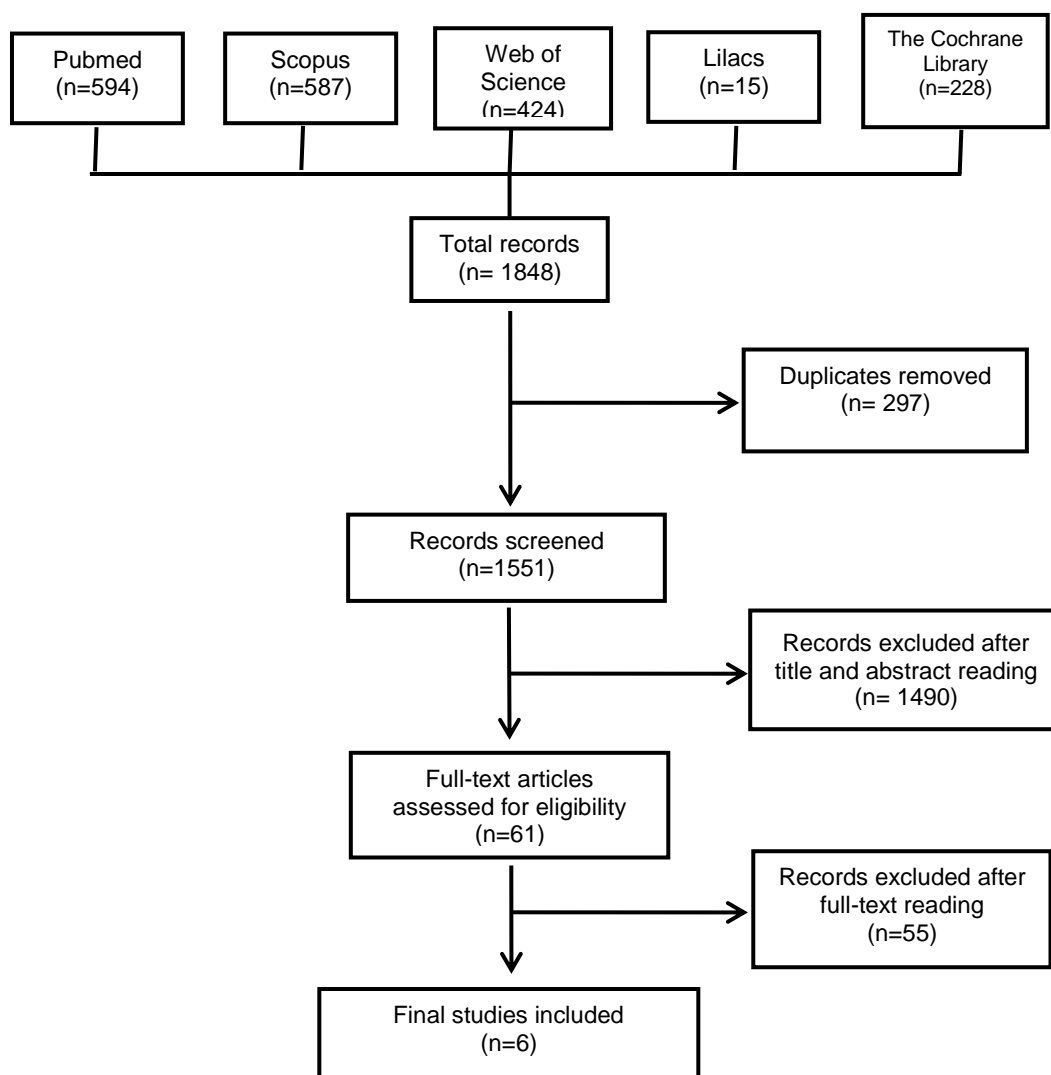


Figure 1. Flow diagram of selected studies

No additional article was found in the manual search.

One study¹⁴, with a mean time of 6.2 years of follow-up, did not identify its range (minimum and maximum follow-up). The authors of this article were contacted to provide the required data, but no reply was received.

A detailed summary of the final selected studies can be found in Table 2. In the absence of controlled trials, our systematic review was based on prospective and retrospective studies.

Table 2. Characteristics of the included studies.

Author/y	Study design	N teeth/ N patients / age of patients	Donor teeth type	Root formation	Follow-up
Mendoza et al. 2012	RS	12/12/9-13y	mx and md PM	½; ¾ and complete root length	10 - 14y
Gonnissen et al. 2010	RS	73/59/11-46y	67 mx impacted can; 3 md impacted can; 2 md molars	½ to ¾; more than ¾; complete root formation	6 - 14y (mean 11y)
Watanabe et al. 2010	RS	38/32/10-43y	mx and md incisors, PM and molars	complete	6.1 - 14.5y (mean 9.2y)
Czochrowska et al. 2002	RS	33/ 28/ 8-15y	2 mx lateral incisor 10 mx PM 16 md PM 2 supernumerary teeth	incomplete	17 - 41y (mean 26.4y)
Paulsen et al. 1995/ Paulsen and Andreassen 1998	PS	118/NR/NR	mx and md PM	3 4 to 4 4 root development with an open apical foramen	6 - 16y (1995) / 6 - 18y (1998)

RS= retrospective study; PS= prospective study; N= number of; y= year; mx= maxillary; md= mandibular; PM= premolar; can = canine, NR = not reported

The studies of Paulsen et al.¹⁹ and Paulsen and Andreassen⁶ used the same patients, however some of the outcomes analysed were different and the follow-up in the second is longer.

In the study performed by Gonnissen et al.¹⁵, the autotransplantations were basically used to correct the position of ectopically impacted canines. The other researchers used autotransplantations to replace missing teeth.

Although the study of Mendoza et al.¹⁶ was defined by the authors as a case series, we considered it a retrospective study, and it was included in our systematic review as so.

The survival rate, mobility rate, pulp condition and root resorption rate from individual studies are summarized in Table 3.

Table 3. Survival rate, mobility rate, pulp condition and root resorption rate from individual studies

Author/y	Survival Rate	Mobility Rate	Pulp Condition	Root Resorption Rate
Mendoza et al. 2012	83.3%	NR	Present teeth(n=10): 100% presented pulp obliteration	<u>Replacement Resorption</u> NR <u>Surface Resorption</u> Present teeth (n=10): 10% <u>Inflammatory Resorption</u> Overall cause of extraction of 2 teeth (16.6%)
Gonnissen et al. 2010	75.3%	Present teeth (n=55): 63.6% - negative mobility 32.7% - normal mobility 3.6% - excessive mobility (Periotest)	Present teeth nontreated endodontically (60%) (n=33): 3% - positive result for cold test 12.1% - positive result for electric pulp test 75.8% - clear pulsatility 57.5% - reduction in size or complete obliteration of pulp chamber	Present teeth (n=55): 38.2% (34.6% - external resorption and 3.6% - internal resorption) Overall cause of extraction of 9 teeth (12.3%)
Watanabe et al. 2010	86.8%	Present teeth (n=33): 18.2% - negative mobility (Periotest)	The quality of root filling was significantly correlated with the success rate (no abnormal findings)	<u>Replacement Resorption</u> Present teeth (n=33): 18.2% Overall cause of extraction of 3 teeth (7.8%) <u>Surface Resorption</u> NR <u>Inflammatory Resorption</u> Present teeth (n=33): 3% Overall cause of extraction of 1 teeth (2.63%)
Czochrowska et al. 2002	91%	NR	In the teeth where pulp obliteration was analyzed (the group compared to contralateral teeth - n=11) 100% showed this alteration	<u>Replacement Resorption</u> Present teeth (n=30): 6.7% Overall cause of extraction of 2 teeth (6%) <u>Surface Resorption</u> NR <u>Inflammatory Resorption</u> NR
Paulsen et al. 1995/ Paulsen and Andreasen 1998	NR	NR	16 teeth (13.5%) showed pulp necrosis and 1 (0.8%) had partial pulp necrosis	<u>Replacement Resorption</u> Present teeth (n= 118): 4.2% <u>Surface Resorption</u> In the teeth submitted to orthodontic rotation (Paulsen et al. 1995) <u>Inflammatory Resorption</u> Presente teeth (n=118): 3.4%

y= year; NR= not reported

The quality evaluation of the articles, in accordance to MINORS¹³, is shown in Table 4. The item was scored “0” when it was not reported, “1” when it was reported and inadequate, and “2” when was reported and adequate.

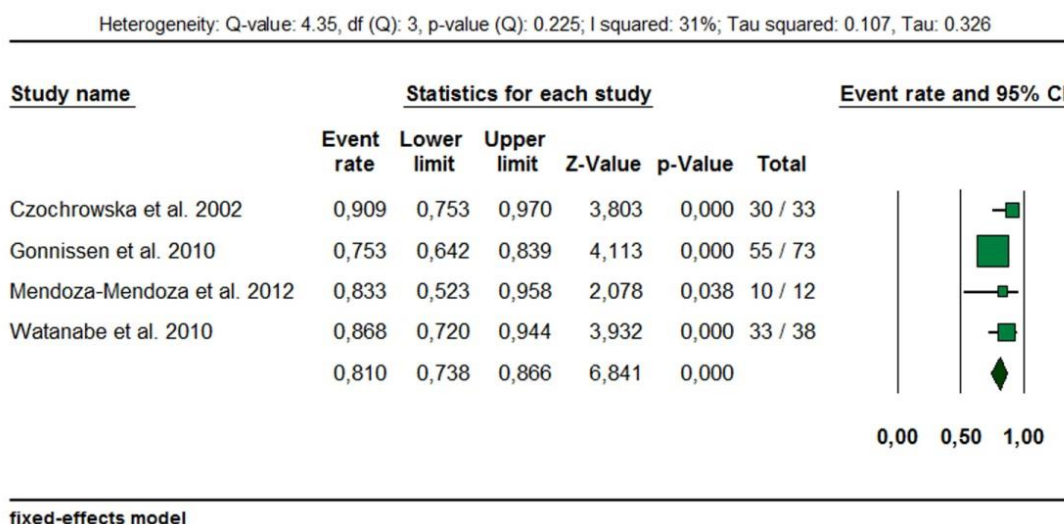
The articles were classified in accordance to their methodological quality as low risk of bias (>17), medium risk of bias (≥ 10 to ≤ 17) and high risk of bias (< 10). All selected studies were classified as medium risk of bias, and were maintained in the present investigation.

Table 4. Score of each article according to the items of MINORS.

Items of MINORS	Mendoza et al.	Gonnissen et al.	Watanabe et al.	Czochrowska et al.	Paulsen et al.	Paulsen and Andreasen
A clearly stated aim	2	2	2	2	2	2
Inclusion of consecutive patients	2	2	2	2	2	2
Prospective collection of data	2	0	0	0	2	2
Endpoints appropriate to the aim of the study	2	2	2	2	2	2
Unbiased assessment of the study endpoint	0	0	0	0	0	0
Follow-up period appropriate to the aim of the study	2	2	2	2	2	2
Loss to follow up less than 5%	0	0	0	0	2	0
Prospective calculation of the study size	0	0	0	0	0	0
An adequate control group	2	0	2	2	0	2
Contemporary groups	2	0	2	2	0	2
Baseline equivalence of groups	1	0	2	2	0	2
Adequate statistical analyses	0	2	1	1	0	0
Total:	15	10	15	15	12	16

The survival rate was mentioned in four studies (Mendoza et al.¹⁶; Watanabe et al.¹⁷; Gonnissen et al.¹⁵; Czochrowska et al.¹⁸), and it ranged from 75.3% to 91%. The meta-analysis provided a significant ($p < 0.0001$) effect size of 81%. The heterogeneity among the studies was low (Table 5).

Table 5. Forest plot of the survival rate.



The percentage of abnormal mobility in transplanted teeth was reported in only 2 studies (Gonnissen et al.¹⁵ and Watanabe et al.¹⁷). Gonnissen et al.¹⁵ found that 63.3% of the teeth had negative mobility and 3.6% had excessive mobility. Watanabe et al.¹⁷ only mentioned that 18.2% had negative mobility, what was in accordance with the percentual of ankylosed teeth.

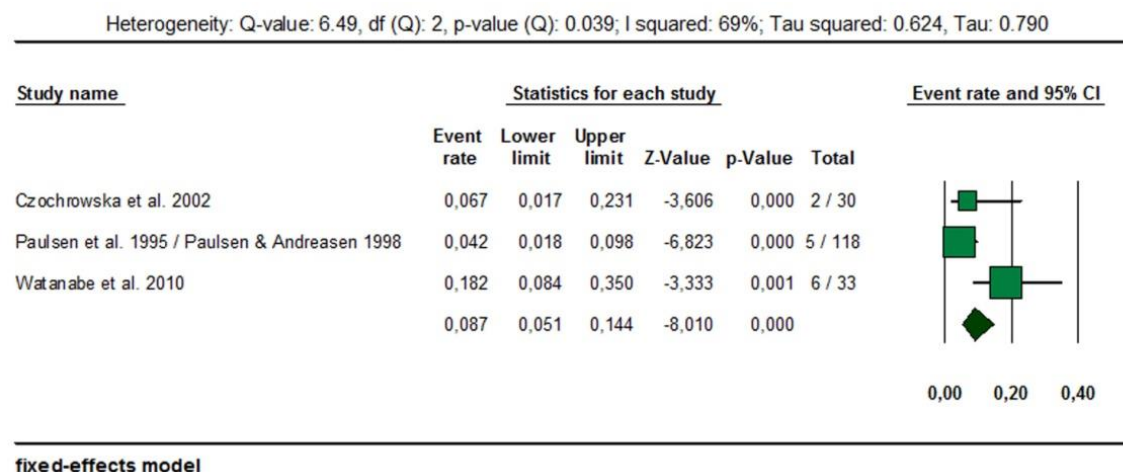
All studies reported the pulp conditions of the transplanted teeth. In 2 studies early endodontic treatment was performed (Gonnissen et al.¹⁵ and Watanabe et al.¹⁷). In the study by Gonnissen et al.¹⁵, early endodontic treatment was applied to patients with more than 20 years of age who had canines with closed apex. In the study performed by Watanabe et al.¹⁷, all teeth were submitted to an early endodontic treatment, in which calcium hydroxide was used to temporarily fill the roots.

In the study by Mendoza et al.¹⁶, Czochrowska et al.¹⁸ and in the teeth nontreated endodontically of the study performed by Gonnissen et al.¹⁵, 100%, 100% and 57.5% of the analyzed teeth, respectively, showed sign of pulp obliteration.

The percentage of replacement resorption (ankylosis) in transplanted teeth was described in four studies (Watanabe et al.¹⁷; Czochrowska et al.¹⁸; Paulsen and Andreasen⁶ and Paulsen et al.¹⁹), ranging from 4.2% to 18.2%. This complication

was the cause of extraction in 7.8% of the teeth evaluated by Watanabe et al.¹⁷ and in 6% of the teeth evaluated by Czochrowska et al.¹⁸. The meta-analysis provided a significant ($p < 0.0001$) effect size of 8%. However, the heterogeneity among studies was considerable (Table 6).

Table 6. Forest plot of ankylosis.



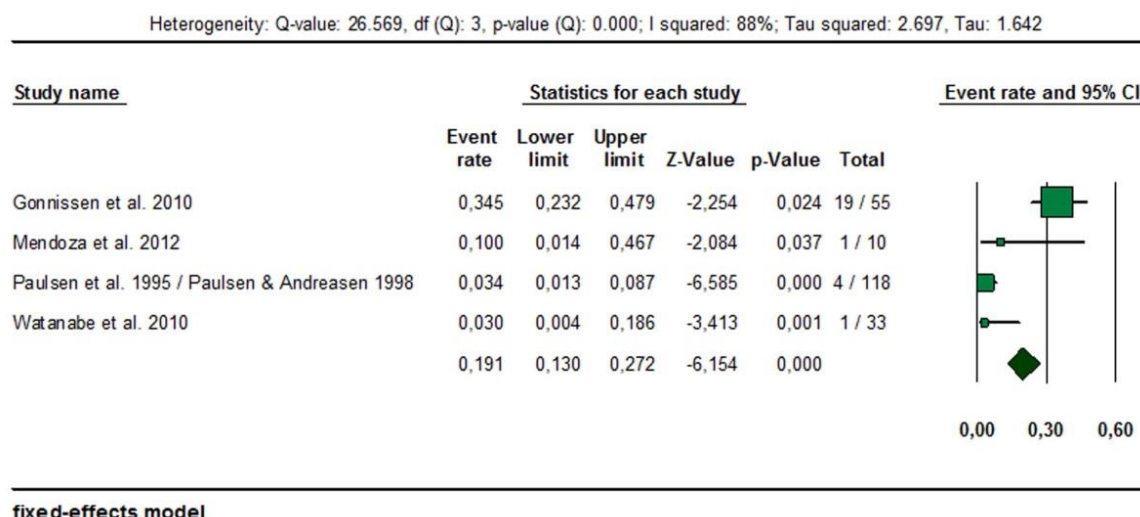
Surface resorption was observed in only one tooth in the study performed by Mendoza et al.¹⁶ and in all the teeth which suffered orthodontic rotation in the study by Paulsen et al.¹⁹.

Inflammatory resorption was observed in the teeth evaluated by Watanabe et al.¹⁷, Paulsen et al.¹⁹ and Paulsen and Andreasen⁶, ranging from 3% to 3.4%. This complication was the overall cause of extraction of 2 teeth (16.6%) in the study by Mendoza et al.¹⁶, and one tooth (2.63%), in the study of Watanabe et al.¹⁷.

In the study by Gonissen et al.¹⁵, 34.6% of the teeth showed external root resorption. This was the cause of extraction of 12.3% of the transplanted teeth. However, the authors do not specify which type of resorption occurred.

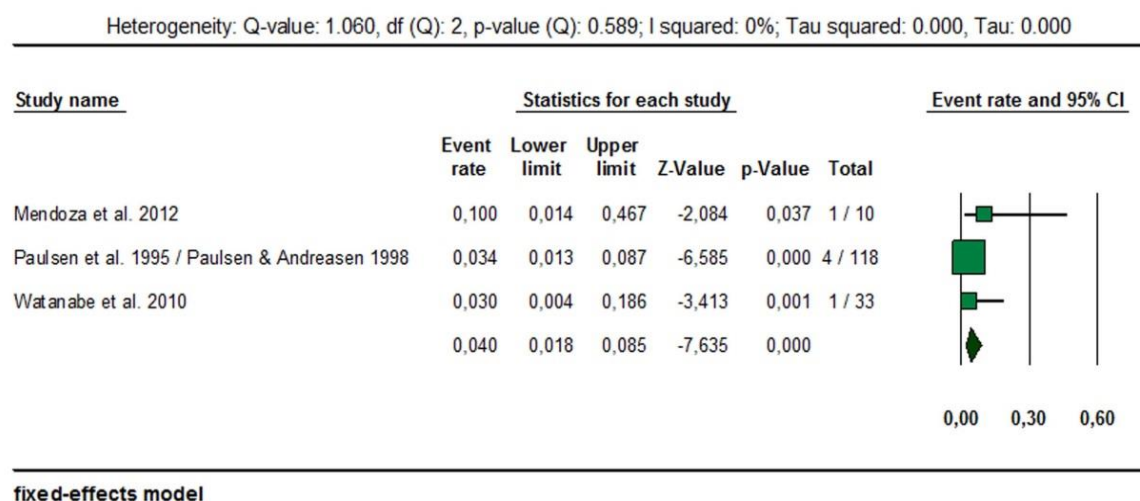
When surface resorption, inflammatory resorption and external root resorption were considered altogether in the meta-analysis, a significant ($p < 0.0001$) effect size of 19% was observed. The heterogeneity among studies, nevertheless, was extremely high (Table 7).

Table 7. Forest plot of resorption



When a sensitivity analysis suggested the removal of the study of Gonnissen et al.¹⁵ from the meta-analysis, the heterogeneity decreased considerably and a significant ($p < 0.0001$) effect size of 4% was observed (Table 8).

Table 8. Forest plot of resorption after sensitivity analysis.



In the perspective of donor teeth type, premolars were used in all studies, except in the study performed by Gonnissen et al.¹⁵, where 70 impacted canines and 2 molars were autotransplanted.

Two studies used premolars and other types of teeth. Czochrowska et al.¹⁸ used maxillary lateral incisor and supranumerary teeth. Watanabe et al.¹⁷ used molars and incisors.

Overall, the analyzed data was based on three studies (Czochrowska et al.¹⁸; Paulsen and Andreasen⁶ and Paulsen et al.¹⁹) with incomplete root formation, one

(Watanabe et al.¹⁷) with complete root formation and other two studies (Mendoza et al.¹⁶ and Gonnissen et al.¹⁵) in which teeth with complete and incomplete root formation were transplanted.

DISCUSSION

This systematic review is a data collection of the prognosis of autotransplanted teeth with a follow-up equal to or greater than six years. Prospective and retrospective studies with stringent inclusion criteria were included to summarize the available information about survival rate, pulp conditions and the percentage of abnormal mobility and root resorption.

Another systematic review¹² has already been published recently. However, it differed from our objective since the authors analyzed the outcomes of autotransplanted teeth only with complete root formation and closed apical foramen. Additionally studies with a follow-up period of at least one year (short-term) were considered. The first-year outcome rate, annual failure rate and 5-years estimate survival rate were evaluated.

In our research, a point that needs to be considered is that four studies are retrospective (Mendoza et al.¹⁶; Gonnissen et al.¹⁵; Watanabe et al.¹⁷; Czochrowska et al.¹⁸). There is no information concerning patients that failed to respond to the recall due to loss of the transplanted teeth. This fact could potentially influence the findings.

When the survival rate was considered, the meta-analysis provided a mean effect of 81%, which is an excellent prognosis, considering that the studies included presented a minimum follow-up of six years.

A mean effect of 8% of ankylosed teeth was pointed by the meta-analysis. In this comparison, however, the heterogeneity was considerable. One of the studies which showed greater discrepancy to the others as well as different methodology, was the one from Gonnissen et al.¹⁵. The authors did not report the percentage of ankylosis directly, but they asserted that negative mobility values pointed toward this condition. The higher percentage of ankylosed teeth observed can be easily explained. The study involved basically impacted canines and some of them were already ankylosed at the time of transplantation. The periodontal ligament does not

exist in some areas in ankylosed teeth and may be thinner and more fragile in impacted teeth¹⁵. Furthermore, the accessibility during the surgery to extract impacted teeth is poor; therefore, the chance of root surface damage is higher. According to Andreasen et al.¹¹, clinical signs of ankylosis can be found within a year after tooth autotransplantation. It is important to know if this process continues along the years in autotransplanted teeth and the long-term percentage of loss. Tsukiboshi⁷ concluded that ankylosis is irreversible and will progress until the loss of the tooth. However, in the study by Czochrowska et al.¹⁸, two ankylosed teeth that had become ankylosed shortly after the surgery, according to available information, were present 17 and 28 years after transplantation. Tsukiboshi⁷ and Czochrowska et al.¹⁸ agree that in ankylosed teeth the gradual progressive resorption can vary with age, being very active in children and significantly slower in adults, in which the affected teeth may survive 10, 20 or more years.

Inflammatory root resorption was observed in four studies (Mendoza et al.¹⁶, Watanabe et al.¹⁷, Paulsen et al.¹⁹ and Paulsen and Andreasen⁶). In the study by Mendoza et al.¹⁶, inflammatory root resorption was found in teeth with no obliteration in the apical region and was the cause of extraction. However, this condition was not clearly explained, once it occurred many years after normal healing. The teeth were extracted 6 and 10 years after transplantation. Nevertheless, it is difficult to explain many years of good healing, indicating the existence of a cementum/cementoblast layer, suddenly followed by resorption, which suggests its absence. In the study by Watanabe et al.¹⁷, inflammatory resorption was the cause of extraction of one tooth with inadequate root filling. So, when periodontal tissue damage can be clinically seen, it could be interesting to perform endodontic treatment some weeks after transplantation, to prevent inflammatory resorption, even with the risk of ankylosis.

Surface resorption was found in only one tooth in the study by Mendoza et al.¹⁶. It was observed in the first 6 months and thereafter remained stable throughout the observation period. This complication was also found in the teeth which suffered orthodontic rotation in the study of Paulsen et al.¹⁹, but the extent of apical root resorption was similar to the amount found in previous investigations of orthodontic treatment of nontraumatized teeth. The positive relationship between orthodontic treatment and surface resorption is to be expected.

In the study by Czochrowska et al.¹⁸, two teeth had crown-to-root ratio greater than one, indicating a short root. However, it is not clear if this condition was caused by root resorption or by the arrest of root development.

When surface resorption, inflammatory resorption and external root resorption were combined in the meta-analysis, a mean effect of 19% was observed. However, a sensitivity analysis indicated that the study of Gonissen et al., which observed 34.6% of external root resorption, causing the extraction of 12.3% of the transplanted teeth, was the main responsible for the heterogeneity among studies. The authors do not specify what type of resorption occurred. If ankylosis, which may be described as replacement resorption, was included, the high rate of root resorption may be explained (this study included basically impacted canines, and some of them were already ankylosed at the time of transplantation). When this study was not considered in the meta-analysis, a mean effect of 4% was observed.

Pulp healing demonstrates strong relationship with the stage of root development and to the dimensions of apical foramen at the time of transplantation⁸. In only one of the final selected studies all transplanted teeth had complete root formation (Watanabe et al.¹⁷). They were submitted to an early endodontic treatment and pulp healing could not be checked, making it impossible to compare this aspect.

According to Northway²⁰, when a transplant is responding favorably, a positive response to pulp vitality can be detected 2 to 4 months after transplantation. This is a sign of revascularization, which is generally followed by obliteration of the pulp canal. In the study by Mendoza et al.¹⁶, all transplanted teeth showed pulp obliteration. In the study performed by Czochrowska et al.¹⁸, all transplanted teeth of the group compared with contralateral control teeth also presented signs of pulp obliteration (in the other group this condition was not analyzed). Both studies were done with incomplete root formation teeth (except for one case of Mendoza et al.¹⁶, where the tooth had complete root formation with open apex). A lower percentage (57.5%) of teeth with signs of pulp obliteration was found by Gonissen et al.¹⁵ in the group of endodontically nontreated teeth. However, this group was formed by transplanted teeth with open apex or transplanted teeth with a closed apex in patients under age of 20. Since revascularization appears to be strongly related to the dimension of the apical foramen¹¹, it may not have happened in the teeth with closed apex.

In some researches, the transplanted teeth received orthodontic load. The application of force did not affect the root development of teeth with incomplete root

formation (Mendoza et al.¹⁶) or influenced the long-term prognosis (Watanabe et al.¹⁷). Gonnissen et al.¹⁵ found that 62.5% of the transplants that suffered orthodontic load were classified as successful, while the success rate for all transplanted teeth was 57.5%. Moreover, Paulsen et al.¹⁹ reported a slight resorption surface and shortening of the root in the teeth that underwent orthodontic rotation. Therefore, the influence of orthodontic movement on the transplanted teeth is variable, but of little clinical relevance.

Based in data from prospective and retrospective studies, it was observed that after a follow-up period of six years, at least, the survival rate was excellent (81%). Ankylosis (8%) and root resorption (4%) rates, despite their low values, contribute to influence the prognosis of the autotransplanted teeth. However, it must be remembered that the absence of randomized controlled trials (RCTs) limited the power of the present investigation.

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4 - CONCLUSÕES

Com base em dados coletados de estudos prospectivos e retrospectivos, observou-se que, após um período de acompanhamento de, no mínimo, seis anos, a taxa de sobrevivência foi excelente (81%). As taxas de anquilose (8%) e reabsorção radicular (4%), apesar de pequenas, contribuem para influenciar o prognóstico dos dentes autotransplantados. Entretanto, deve-se considerar que a ausência de estudos clínicos randomizados limita o poder da presente investigação.