Systematic Review

Autogenous transalveolar transplantation of maxillary canines: a systematic review and meta-analysis

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Summary

Background and objectives: The objective was to systematically review transalveolar transplantation of maxillary canines and the long-term outcome for an average follow-up period of 2 years or more.

Data collection and analysis: A systematic review of the currently available literature until December 2017 was conducted, using Medline, Cochrane Central, Web of Science, and PubMed. Articles were screened for 1. indications, 2. contra-indications, 3. surgical planning, 4. surgical technique, 5. associated risk factors, and 6. long-term outcome for transalveolar transplantation of maxillary canines with the following outcome measures: bone-related outcomes, tooth-related outcomes, soft tissue-related outcomes, and aesthetic outcome measures. Descriptive statistics, as well as a quality assessment of included articles, were performed. Following study retrieval and selection, relevant data was extracted and the risk of bias was assessed using the Methodological index for non-randomized studies (MINORS).

Results: Twelve articles were included in this review. These studies included outcome data for 783 autotransplanted maxillary canines, with long-term studies indicating a clinically acceptable overall outcome.

Limitations: Since the lack of randomized controlled trials considering this topic, the quality of the evidence in the present review is considered low. However, impacted maxillary canines are a rare anomaly and different aspects, such as position of the impacted canine, patient’s age and patient’s demands, and expectancies must be taken into account, it is practically impossible to randomize treatment.

Conclusions: There is sufficient evidence to justify the transalveolar transplantation of maxillary canines as a legitimate treatment technique for impacted maxillary canines deemed difficult to treat with surgical exposure and subsequent orthodontic alignment. Long-term studies have shown that a good overall outcome is to be expected. There is no clear agreement in the literature on the indications and contra-indications for transalveolar transplantation of maxillary canines.

Implication of key findings: It is highly desirable that further research on this issue be undertaken, high-quality observational studies are recommended.

Registration: PROSPERO (CRD42017056348)
Introduction
Impaction is defined as failure of tooth eruption at its predetermined site in the dental arch, within its normal period of growth, due to an obstacle in the eruption path or ectopic position of the tooth germ (1).

Permanent maxillary canines are the second most frequently impacted teeth with an incidence ranging from 0.9 to 2.2 per cent, the most frequent being wisdom teeth (2). Impaction of permanent maxillary canines occurs three times more often in females than in males. Eight to ten per cent of these cases are bilateral (3). Untreated partially erupted or impacted canines may result in several complications such as displacement and loss of vitality of the adjacent incisors, shortening of the dental arch, formation of follicular cysts, canine tooth ankylosis, recurrent infections, pain, internal resorption, external resorption of the canine and adjacent teeth, or combinations of these factors (4).

Initially, diagnosis of impacted maxillary canines is clinical, with attention for distal displacement or distal inclination of the lateral incisor (ugly duckling), lateral incisor mobility, retention of the primary canine in the dental arch beyond the age of 14-15, palatal swelling, or absence of the typical vestibular prominence (5). Further radiographic analysis with panoramic radiographs (PR) and cone-beam computed tomography (CBCT) is essential for the assessment of canine position and to detect canine root malformations, local obstructing pathology, or incisor root resorption.

Traditional treatment options for impacted canines are 1. interceptive removal of the deciduous canine, 2. surgical exposure with or without orthodontic traction to align the malpositioned tooth, 3. no treatment, 4. autotransplantation of the permanent canine, or 5. removal of the permanent canine and prosthetic or restorative treatment. When surgical exposure and subsequent orthodontic realignment are difficult or impossible because of an unfavourable canine position, autotransplantation is a valuable alternative to extraction or other treatment options. High positioning or an angulation larger than 45 degrees relative to the occlusal plane are known selection criteria of autotransplantion (6). Orthodontic treatment is not always accepted by patients because treatment time may increase to 2–3 years, depending on many factors such as the canine position, aesthetic, and economical considerations. In such cases, and with sufficient diastema, autotransplantation of the maxillary canine may be a good treatment.

So far, no systematic reviews assessing indications for transvleolar transplantation of maxillary canines and their outcomes over the long-term have been reported in the literature. In this study, the aim was to systematically analyse the scientific literature regarding transvleolar transplantation of maxillary canines considering 1. indications, 2. contra-indications, 3. surgical planning, 4. surgical technique, 5. associated risk factors, and 6. the long-term outcome for transvleolar transplantation of maxillary canines: bone-related outcomes, tooth-related outcomes, soft tissue-related outcomes, and aesthetic outcome measures. Criteria for including studies in this systematic review are shown in Table 1.

Materials and methods
The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were followed to ensure transparency and comprehensiveness in this systematic review (7). A search protocol was specified in advance and registered at PROSPERO (International Prospective Register of Systematic Reviews) nr. CRD42017056348.

Objective
To review transvleolar transplantation of maxillary canines considering 1. indications, 2. contra-indications, 3. surgical planning, 4. surgical technique, 5. associated risk factors, and 6. long-term outcome for transvleolar transplantation of maxillary canines: bone-related outcomes, tooth-related outcomes, soft tissue-related outcomes, and aesthetic outcome measures. Criteria for including studies in this systematic review are shown in Table 1.

PICOS question
Eligibility criteria were determined a priori according to the Participant–Intervention–Comparison–Outcome–Study design (PICOS) scheme (Table 1).

Search strategy for the identification of studies
The search strategy was developed for EMBASE and appropriately adjusted for Cochrane Central, Web of Science, and PubMed. The electronic databases were searched for articles published up until December 2017. The search strategy used a combination of controlled vocabulary and free text terms and was run with the recommended EMBASE and MEDLINE filters to identify randomized controlled trials (8).

The full search protocol for the different databases is displayed in Supplementary Table 1. No language or data restrictions were applied when searching the electronic databases. Additionally, all references of selected full-text articles were manually screened for potentially useful articles.

Data collection and analysis
Selection of studies
Titles and abstracts of relevant studies identified through the electronic searches were screened by three authors (KG, DC, and LPGR). Full-text articles were obtained from the studies that fulfilled the inclusion criteria. These full-text articles, together with full-text articles found through the manual search, were independently assessed by these authors to determine if they were in line with the inclusion criteria. Disagreements were resolved through discussion. After selection, data extraction and a risk-of-bias assessment were performed.

Inclusion and exclusion criteria of eligible studies
Main inclusion criteria
- Studies investigating the indication, success/survival rate, and surgical procedure of autologous transplantation of maxillary impacted canines
- Controlled trials or prospective/retrospective studies, case series with at least 10 transplanted maxillary canines
- Studies reporting at least one of the following: survival rate (short or long-term), success rate, pulp condition, tooth mobility, presence of ankylosis, and root resorption of autotransplanted teeth with complete or incomplete root formation
- Mean follow-up period should be at least 2 years
- No restrictions on language were made
Main exclusion criteria

- Studies including autologous transplantation other than maxillary canines
- Case reports, case series with less than 10 transplanted maxillary canines, opinion articles, and review articles
- Studies reporting autotransplanted teeth in patients with systemic diseases, syndromes, or cleft lip and palate
- Animal studies
- Studies without specified transplantation protocol
- Studies referring to transplantation of traumatized maxillary canines
- Studies reporting autotransplantation of teeth with a history of cysts, tumours, or trauma
- Studies including sterilized teeth, cryopreserved teeth, or teeth maintained in culture media
- Studies with oro-antral fistulae
- Studies examining tooth autotransplantation associated with maxillary sinus lifting
- Studies examining autotransplantation of canines subjected to endodontic treatment during transplantation surgery
- Studies with patients that have genetic or systematic diseases
- Studies not including information about follow-up

Data recorded:
- Methods: study design, location/setting, recruitment period
- Participants: inclusion and exclusion criteria, demographics, number of participants, and autotransplanted maxillary canines
- Intervention: details regarding type of intervention
- Outcomes: bone-related, tooth-related, periodontal, and aesthetic outcome, and average follow-up time

Methodological quality assessment

The assessment of the methodological quality of the articles, in accordance with Methodological index for non-randomized studies (MINORS), is shown in Supplementary Table 2. An item was scored as '0' when not reported, '1' when it was inadequately reported, and '2' when it was adequately reported. The articles were classified according to their methodological quality into low (>17), medium (≥ 10 ≤17), and high risk of bias (<10).

Statistical analysis

Studies were divided into two groups: short follow-up (2–5 years) and long-term follow-up (5 years or more). For every group and success parameter, a meta-analysis based on a generalized linear mixed model for binary outcomes was built using a logit-link. Forest plots for survival analysis 2–5 and 5 years or more were performed (Figures 2 and 3). Horizontal lines next to article names reflect the confidence interval for the parameter under interest for individual studies. The size of the quadrangle in the middle reflects the weight of each individual article in the meta-analysis. The figure in the lower part of the graph shows the confidence interval of the parameter, as obtained by meta-analysis taking into account all mentioned studies.
Risk of bias in included studies
On the basis of the MINORS quality assessment, one study had a low risk of bias, six studies a moderate risk, and five studies a high risk (Supplementary Table 2).

Results
Description of the studies
Results of the search
After screening titles and abstracts of 132 unique papers, 35 potentially eligible articles were selected (Figure 1). Each title and abstract was independently reviewed by two researchers (KG and DC), and the obtained information was compared. Inter-examiner disagreements were resolved in a consensus meeting. Of the 35 potentially eligible articles, 23 were excluded. These articles were excluded for the following reasons: study with histological analysis; studies concerning autotransplantation without specific results or conclusions about maxillary canines; short paper about general reasons, requirements, treatment plans, and techniques of autotransplantation of maxillary canines without clinical outcomes; studies with preoperative endodontic treatment; studies with systematic surgical exposure of the maxillary canine before autotransplantation; studies focusing on root anomalies of impacted maxillary canines; case series with less than 10 transplanted maxillary canines; literature reviews; studies without information about survival and/or success rates and one study with no report of the surgical procedure, follow-up modalities, or even outcomes.

Included studies
A total of 12 articles were identified for inclusion in this review (9–18). This systematic review was based on prospective and retrospective cross-sectional studies and case series due to the absence of controlled trials. The reported final outcomes, ankylosis, and root resorption rates from individual studies are summarized in Table 2. Information on pre-operative assessment, operative protocol, and post-operative assessment is provided in Supplementary Table 3.

For meta-analysis considering endodontic treatment analysis, four studies were excluded (12–14,20). For analysis of resorption and ankylosis, four (16,17,19,20) and six studies (10,14,16,17,19,20) were, respectively, excluded.

Characteristics of the study settings and investigators
Of the 12 included studies, four were performed in Sweden (9,13,16,17) and two in Australia (11,19). Other studies were performed in Belgium (12), Turkey (10), South Africa (14), UK (15), USA (20), and Switzerland (18). Studies had a retrospective, cross-sectional, retrospective case series, and case–control nature (split-mouth design).

Characteristics of the participants
The mean age of the participants ranged from 19.8 to 36.5 years old (minimum age 11 and maximum age 76). Three studies did not report mean age (13,14,20). The distribution of men and women was presented in 5 of the 12 studies. Between 12 and 113 patients were selected for each study, with a median of 33 patients. Four studies mentioned the number of teeth rather than the number of patients (12–14,20). Fourteen to 162 maxillary canines were selected for each study, with a median of 37 maxillary canines. Nine studies solely reported on the transplantation of maxillary canines (6,9–11,14–17,19). Three studies reported on the transplantation of maxillary canines as a subgroup (12,13,20).

Sample size calculation
None of the studies reported sample size calculations.

Characteristics of the interventions
Pre-operative assessment
Most of the studies did not report any details about clinical and radiographical pre-operative assessment. Root development stage was...
mentioned in three studies and found to be complete in all canines of these studies (9,10,15). Canine positions were mentioned in two studies (9,19). Canine angulation and root anomalies were not mentioned in any studies. Pre-operative orthodontic treatment was discussed in three of the included studies (14,16,17). In three studies, authors mentioned orthodontic treatment pre-operative for widening of the diastema (14,16,17). Radiographical analysis was mentioned in seven studies and performed with 2D images. None of the included studies discussed 3D imaging with CBCT or 3D planning.

Indications for autotransplantation were vaguely described in two studies (16,17). These studies mentioned severe impaction and difficult malpositioning, as such that orthodontic treatment was either impossible or would have been complicated and time-consuming.

Operative protocol

The surgical procedures of maxillary canine transplantation were identical or similar to the protocol demonstrated by Andreasen et al. (21). First, the surgical sites are disinfected and a local anaesthetic is injected. The remaining primary canine, if still present, is extracted, and a trapezoidal flap incision is made ensuring intact mesial, distal, and palatal gingiva at the graft site. To prepare the recipient socket, an osteotomy is performed using a surgical bur with water cooling and chisels. The socket for the graft should be slightly larger than the graft. Next, the crown of the impacted canine is exposed and the tooth removed with a periosteal elevator. The donor tooth is extracted slow and as atraumatically as possible. Next, the donor tooth is placed into the recipient socket without any pressure. The trapezoidal flap is repositioned and sutured.

Six studies mentioned the extra-oral time as: <15, <20, <25 min, ‘brief’, ‘with minimal delay’, or without extra-oral time (10,11,13,14,17,19). Five studies mentioned the storage medium as: cloth saturated with saline (3), in physiological saline or intra-alveolar at the donor site (9,11,13,14,17). The fixation method was discussed in 11 studies as: attached to the orthodontic wire for 3–6, 5, 12, or 3–6 months, to a splint (undefined type) for 2, 4, or 6 weeks, to a plastic vacuform splint or silver splint for 4 weeks, to a metal cap splint for 6 weeks or with sutures for 2 till 3 weeks (6,9–12,14–17,19,20). Occlusal positioning of the transplanted maxillary canine was discussed in 11 studies and found to be infra-occlusal in 5 studies and functional in 6 studies (6,9–12,14–17,19,20).

Post-operative assessment

Most of the studies did not report any details about the post-operative assessment other than including clinical and radiographic examinations. In none of the studies a clear healing protocol was discussed. One study mentioned a minimal delay of 1 year for instrumentation of the periodontium (10). The duration and recurrence of clinical and radiological follow-up were mentioned in, respectively, five and eight studies (Supplementary Table 3). Two studies mentioned orthodontic treatment post-operatively but did not discuss timing (14,17). Endodontic treatment and indications were discussed in all 12 studies. In four studies, endodontic treatment was a standard protocol after transplantation (10,11,16,17). In seven studies, endodontic treatment was only indicated in case of signs of periapical infection or inflammatory root resorption (9,12–15,19,20). In one study, endodontic treatment depended on patient’s age and root formation (6).

Characteristics of outcome measures

Some studies define outcome differently by using various success and survival criteria in which only teeth without any signs of resorption and/or endodontic treatment can be considered to be successful.
However, it should be questioned whether root resorption observed after tooth transplantation constitutes a failure when it is possible to keep the tooth in place for a prolonged time without further bone resorption and on the contrary even maintain the alveolar ridge by the process of replacement resorption (22,23). As such, authors of this review preferred to use calculation of a general outcome in which successful outcome was defined as the percentage of transplanted teeth still present and functioning well at the time of recall. Failure was defined as loss of the autotransplanted maxillary canine during the observation period.

Infection-related root resorption was defined as the autotransplanted tooth exhibiting resorption signs on a radiograph. Ankylosis was defined as the absence of clinical mobility with or without root resorption on a radiograph. The data of failure, infection-related root resorption, and ankylosis were based on the reported results from the original articles.

Bone-related outcomes were seldom explicitly reported, except for vertical bone loss in six studies, and the presence of lamina dura in three studies (Supplementary Table 3).

Tooth-related outcomes were more frequently reported. Nine studies discussed the prevalence of root resorption and two studies discussed changes in pulp chamber appearance. Seven studies reported testing of tooth vitality and four studies compared tooth colour. Four studies tested tooth mobility and subsequently also ankylosis, in nine studies frequency of endodontic treatment was discussed (Table 2).

Soft tissue outcomes were frequently tested by all studies in the clinical follow-up. Nine studies checked the periodontal attachment by controlling the pocket depth (6,9–12,15–17,19). Only one study mentioned a 1-year healing interval before probing (10). Four studies evaluated gingival recession levels and two studies evaluated the periodontal space (Supplementary Table 3).

Aesthetic outcome was reported in two studies by means of patient satisfaction (11,16). No objective criteria were used to score the aesthetic outcome in none of the included studies.

### Duration of mean follow-up

The duration of mean follow-up was found in seven studies. In two studies, only a minimal follow-up time was mentioned (14,20). In those cases, minimal follow-up time was used for further calculations. In three studies, autotransplanted maxillary canines were subdivided regarding mean follow-up time (11,14,19). Only subgroups with a mean follow-up time of minimal 2 years were included. In case of multiple subgroups with a mean follow-up time of minimal 2 years, only the subgroup with the most complete amount of follow-up information was included. The data of the mean follow-up times were based on the reported data from the original articles.

### Calculations performed on data

Meta-analytic results are summarized in Table 3. The meta-analysis showed a final outcome rate of 87.5 per cent (CI 77.1; 93.6) in the short-term follow-up group (2–5 years) and 88.2 per cent (CI 81.4; 92.7) in the long-term follow-up group (>5 years). Endodontic treatment was calculated to be performed in 82.5 per cent (CI 31; 98) of the canines in the short-term follow-up group (2–5 years) and 91.5 per cent (CI 53.3; 99) of the canines in the long-term follow-up group (>5 years). The meta-analysis showed the complication rate of root resorption and ankylosis to be, respectively, 18.5 per cent (CI 7.4; 39) and 23.8 per cent (CI 4.8; 65.7) in the short-term follow-up group (2–5 years) and 32.3 per cent (CI 5.4; 74.9) and 65.2 per cent (CI 0.2; 99.9) in the long-term follow-up group (>5 years) (Figures 2–3).

### Effects of intervention

Twelve studies presented outcome data for 783 autotransplanted maxillary canines. Results for all outcomes are summarized in Table 2.

### Discussion

#### Summary of evidence

This systematic review is the first comprehensive meta-analysis of autotransplanted maxillary canines. The objective of this study was to review transalveolar transplantation of maxillary canines and long-term outcome. Investigated outcome parameters included degree of mobility, pulp, and root conditions and final aesthetic outcome for a follow-up period of 2 years or more. Prospective and retrospective studies identified in accordance with strict inclusion criteria were included. Information available on indication and follow-up were summarized. In total, 12 studies were included in the review.

In the current review, it was evident that the literature lacks sufficiently well-organized studies concerning the topic of autotransplantation of maxillary canines. There was a striking absence of clear-reported diagnostic pathways, pre-operative planning, and post-operative follow-up. Concerning the surgical technique, there is more uniformity between the different studies. None of the studies explicitly reported careful handling of the follicle. None of the reviewed studies mentioned 3D planning. None of the reviewed studies mentioned an objective evaluation of the final result.

An effort was done to include high-quality studies. However, most studies were retrospective. The level of bias in retrospective studies may be very high, which indicates the need for better designed studies addressing this subject. Organizing randomized controlled trials about this topic would be difficult as controls have different initials situations.

### Overall completeness and applicability of evidence

This review included one case-control, six retrospective, and five cross-sectional studies on the transalveolar transplantation of...
maxillary canines (Table 2). Considering a small number and retrospective study design of most studies, there is still insufficient evidence to support definitive conclusions.

None of the included studies reported adequate guidelines for pre-operative clinical and radiographical assessment and orthodontic pre-treatment. Most of the studies reported the use of 2D radiographs for evaluation of the status of root and apex and canine position. However, none of the included studies reported canine angulation and root anomalies. None of the included studies reported the use of 3D radiographic analysis with CBCT. At the time when most of the referred studies in this systematic review were performed, CBCT data was not yet introduced in clinical routine, with treatment planning and follow-up mostly based on 2D radiographs and clinical examination. Furthermore, for such procedures, the use of 3D data and CBCT is most often not advocated in case of (long-term) follow-up, unless problems. More recently there is a tendency to use 3D planning for autotransplantation enabling accurate positional planning, increasing the ease of surgery, and decreasing the extra-oral time. However, the quality of the existing body of evidence is low. Further research is therefore required to investigate the clinical advantages of this innovative autotransplantation technique. When integrating CBCT examinations in the planning and follow-up, one should be aware of the costs and the radiation patients are exposed to. Also CBCT do not necessarily provide more information compared to intra-oral radiography (24).

The surgical protocol was defined in all the included studies. All of the studies followed the same surgical technique, minimalized the extra-oral time of the extracted canine and, when reported, used physiological saline or intra-oral storage. The fixation method varied in length (2 weeks–6 months) and method (sutures, orthodontic wire, plastic vacuform splint, metal cap splint).

The post-operative assessment was only reported more extensively in few studies. Most of the studies only mentioned the duration and recurrence of clinical follow-up and the usage of 2D radiographs. Most authors consider endodontic treatment of autotransplanted canines with closed apices as mandatory analogue of traumatically avulsed teeth with closed apices. In cases of immature teeth with open apices, a wait-and-see strategy is accepted due to the considerable potential of revascularization. However, some authors also suggest a wait-and-see strategy even in cases of closed apices.

Better survival and success rated have been reported with autotransplanted teeth with open apex versus closed apex. However, Chung et al. (25), in their systematic review of transplanted teeth with a closed apex, found high survival rates of 98 per cent at the 1-year follow-up point and 90.5 per cent at the 5-year follow-up point. Acevedo et al. (26), in their systematic review of teeth with an open apex found a survival rate of 98 per cent after a mean follow-up period of 6 years. In a recently published long-term follow-up case series, Murtadha et al. (27) concluded that one might need to reconsider the protocol of routinely providing endodontic treatment for transplanted teeth with closed apices, because some might have the potential for revascularization.

None of the included studies discussed orthodontic movement after surgery. Most of the included studies reported on only tooth-related outcomes such as tooth survival, root resorption, and ankylosis. However, only the minority of the included studies reported a complete clinical evaluation including changes in pulp chamber, canine

| Study                  | Log Odds |
|------------------------|----------|
| Kvint et al            | 2.23 [1.04, 3.42] |
| Lownie et al           | 1.18 [0.66, 2.30] |
| Pogrel et al           | 0.48 [0.16, 0.79] |
| Sagne et al (1986)     | 3.37 [0.55, 6.19] |
| Schatze et al          | 3.66 [0.86, 6.47] |
| Chambers et al         | 2.97 [1.55, 4.39] |
| Hall et al             | 2.21 [1.65, 2.76] |
| Kallu et al            | 2.12 [1.27, 2.97] |

Figure 2. Forest plot survival 2–5 years.

| Study                  | Log Odds |
|------------------------|----------|
| Patel et al            | 1.55 [0.90, 2.20] |
| Ahlberg et al          | 3.47 [1.48, 5.46] |
| Arikan et al           | 2.71 [1.28, 4.14] |
| Sagne et al (1997)     | 2.00 [1.40, 2.61] |

Figure 3. Forest plot survival 5 years or more.
Based on the findings of the current study, it became clear that the Implications for practice

It is suggested that future studies should focus on indications for autotransplantations of maxillary canines, long-term clinical success parameters, revisit surgical techniques, 3D planning, (long-term) aesthetic results, and patient satisfaction.

Supplementary material

Supplementary materials are available at European Journal of Orthodontics online.

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Conflict of interest

None to declare.

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