Controversies Regarding the Management of Teeth Associated with Cystic Lesions of the Jaws

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The continual growth of cystic lesions of the jaws can cause bone expansion, facial deformity, impacted teeth, occlusal disorder and displacement and loosening of the originating tooth or adjacent teeth. The management of teeth associated with cystic lesions of the jaws has been widely debated. When standing teeth with vital pulp are associated with cystic lesions, especially when tooth roots protrude into the cyst cavity, different treatment options have been recommended to support tooth preservation. However, there is no consensus about the extraction of the affected tooth in cases of root involvement by odontogenic keratocyst (OKC). In addition, there is controversy around whether root canal therapy should be considered a necessary treatment to be carried out prior to or after enucleation when standing teeth are associated with cystic lesions. An impacted tooth enclosed in the cavity of a developmental cyst may be treated by various approaches such as marsupialisation or decompression, or enucleation in combination with extraction or coronectomy, depending on the patient's age, root development and the angle and depth of the tooth in the jaw. Successful results obtained in pulp revascularisation after autotransplantation or endodontic regeneration treatments have been reported and pulp tissue functionality after cyst enucleation or apicetomy is a serious concern. In this article, we present an overview of the management of teeth associated with cystic lesions of the jaws.

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A cyst is defined as a pathological cavity having fluid, semi-fluid or gaseous contents and frequently enveloped by an epithelial tissue membrane, but not created by the accumulation of pus[1,2]. This definition does not require the presence of an epithelial lining as being essential for a diagnosis. It also recognises that a number of lesions not of epithelial origin are cystic and are commonly included in the classification of cysts[3]. Therefore, cystic lesions of the jaws may be epithelium lined or nonepithelium lined, odontogenic or nonodontogenic and developmental or inflammatory in origin[4,5].

The clinical features of jaw cysts are characterised by slow growth and asymptomatic expansion, unless secondarily infected or very large. Expansion of bone is commonly observed at the buccal cortex, but in very large cysts both buccal and lingual cortices may be noticeably expanded. Odontogenic cysts are the most common cause of jaw expansion and tooth displacement, but these changes are also observed in nonodontogenic cysts and cystic odontogenic tumours[6-9].

Imaging modalities used in the evaluation of cystic lesions of the jaws include intraoral radiography, panoramic tomography, cone beam computed tomography (CBCT), computed tomography (CT), magnetic resonance imaging (MRI) and ultrasound (US). Nowadays, CBCT is often used in oral and maxillofacial surgery by providing an accurate evaluation and treatment plan prior to the surgery. This new imaging modality introduces a three-dimensional (3D) image in one rota-

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tion only, with a lower radiation dose and a simpler technique than multidetector CT (MDCT)[10]. Such multiplanar views can obtain important information on the details of lesional bone changes and the relation of the cyst to the adjacent anatomic structures, which can enhance the quality of the diagnosis and preoperative assessment of cystic lesions of the jaws[11,12].

Treatment for cystic lesions depends on the size, location, patient age, perforation of cortical layer and proximity to vital structures such as teeth, the inferior alveolar canal, nasal cavity and maxillary sinus[13-21]. Teeth involved in the cystic lesion are generally removed during enucleation. However, there is still no consensus about whether the standing teeth involved need to be extracted or treated by root canal therapy with apicoectomy, especially odontogenic keratocyst (OKC) or keratocystic odontogenic tumour (KCOT), since these cysts tend to recur more frequently than other odontogenic cysts and have a more locally aggressive behaviour[4,22,23]. Recurrent OKCs may be due to the incomplete removal of the epithelium around the tooth roots that extended into the cyst cavity. The removal of the affected teeth or treatment with apicoectomy is recommended if the roots extend into the cyst lumen and interfere with the complete removal of the cyst wall[24]. Some research has suggested that marsupialisation or decompression at the first stage followed by enucleation minimised the damage to adjacent structures and reduced the recurrence rate when used for large or extensive OKCs[15,25,26]. Therefore, it seems appropriate to perform this two-stage surgery if multiple teeth are involved in the event of OKCs.

Dentigerous cysts are frequently associated with impacted teeth, especially mandibular third molars. Where surgical intervention is indicated, the most common treatment modality is enucleation with the removal of impacted tooth; however, in some cases, marsupialisation may precede this[27,28]. A permanent tooth in a dentigerous cyst in preadolescents often erupts successfully after marsupialisation and resolution of the cyst[16,29]. Large cystic lesions are marsupialised initially or in combination with orthodontic traction and then enucleated at a later stage, facilitating the tooth's extraction and reducing the possibility of iatrogenic damage to adjacent structures or the need for jaw resection[30-34]. In some cases of dentigerous cysts where deeply impacted teeth have been deemed to be in close proximity to the inferior alveolar nerve, coronectomy is an elective procedure that involves careful removal of the crown of the tooth while maintaining the roots, with the decreased risk of nerve injury or mandibular fracture[35].

The term 'revascularisation' originated from the dental trauma literature. In some cases, a tooth with incomplete root formation may be able to reestablish blood supply after autotransplantation or replantation. Angiogenesis is the predominant process during pulp regeneration and autotransplantation[36]. The driving force of angiogenesis is hypoxia[37], which can be seen in pathological situations where the pulp tissue is subjected to oxygen supply disruption such as carious/traumatic pulp injuries, tooth autotransplantation and replantation or pulp regenerative treatment. Different treatment options have been considered in the management of cystic lesions to support tooth preservation[16,38-41] and pulp tissue functionality after cyst enucleation or apicetomy is a serious concern. However, there is controversy around whether root canal treatment should be considered a necessary treatment, either prior to or after enucleation, when standing teeth are involved in the cystic lesion. In this article, we present an overview of the management of teeth associated with cystic lesions of the jaws based on our experiences and those of other practitioners in the literature.

Evaluation of cystic lesions and involved teeth

Clinical evaluation

Depending on the size of the lesion, cystic lesions of the jaws are usually asymptomatic and may be detected incidentally via routine radiographic examination or when they are large enough to cause facial asymmetry[21,27]. The clinical absence of one or more teeth from the normal series in an otherwise complete dentition without a history of extraction may imply the presence of a dentigerous cyst[1,4]. A single missing tooth together with a cystic swelling may also indicate the existence of an OKC. Clinical signs suggestive of a dentigerous cyst include a retained primary tooth, delayed eruption of a permanent tooth and painless swelling of the involved area. The teeth adjoining an OKC or a dentigerous cyst will have vital pulp unless there is coincidental disease of these teeth. Periapical cysts are associated with pulp necrosis. It is important to emphasise that cysts or cystic lesions with infection might show a rapid pain expansion, and extensive lesions may result in pathological mandibular fractures and deformation of the jaws. The expansion of cystic lesions may produce impingement on surrounding structures such as the inferior alveolar nerve and the roots of adjacent teeth, resulting in paresthesia, displacement and root resorption. Cystic lesions may displace or obliterate the maxillary sinus, nasal cavity and orbital cavity, which leads to diplopia[1,42].

Imaging evaluation

The classic radiological appearance of an odontogenic cyst in the jaws is a well-defined, round or oval area of radiolucency, circumscribed by a sharp radiopaque margin[1,7]. Dentigerous cysts appear as a well-defined unilocular radiolucency associated with the crown of an unerupted tooth. Often, the radiolucent area surrounds the crown, but sometimes it lies mainly or entirely to one side. A radicular cyst is a well-defined radiolucency associated with the apex of a nonvital root or tooth. However, there are many variations to this standard pattern, which depend on the cyst type, location, degree of bone destruction and expansion or secondary infection. Panoramic radiography and periapical films are the backbones of diagnostic imaging. However, ordinary radiography has several limitations such as the superimposition of anatomical structures and the inability to detect small changes in bone density.

CT, CBCT and MRI are useful techniques for evaluating the topography of cystic lesions, the integrity/discontinuity of bony margins, dimensions, the exact anatomical site of lesions, the proximity to vital structures and the displacement of teeth[6,11,43,44]. CBCT images are not distorted or enlarged, and have a margin of error of < 0.1 mm. In contrast, one multislice CT scan has a margin of error of 1.0 to 1.5 mm[45]. The usual exposure dose of CBCT is 40 to 60 times lower than that of multislice CT[46]. The main advantages of CBCT over conventional CT are its very high spatial resolution, which introduces a 3D image in one rotation with a lower radiological dose and a simpler technique[10,44]. Such multiplanar views provide important information on the presence and extent of lesional bone resorption, sclerosis of the neighboring bone, buccal and/or lingual cortical expansion, internal or external calcifications, resorption of the adjacent teeth roots and the relation to the adjacent anatomic structures. This information can enhance the quality of the diagnosis and the preoperative assessment of cystic lesions of the jaws[9,11,12].

One of the major advantages of MRI over CT and CBCT is its high soft tissue contrast and the possibility of varying the contrast by changing the MRI sequence design. More specifically, MRI not only provides an excellent soft tissue contrast, it also allows for the evaluation of specific tissue components in different sequence types before and after gadolinium administration. A study by Juerchott et al[47] indicates that radiation-free dental MRI enables a reliable differentiation between periapical cysts and granulomas *in vivo*. US has also been used to distinguish periapical cysts from periapical granulomas when there is sufficient thinning of the labial cortex[48].

Pulp vitality testing

Accurate assessment of the pulp vitality or blood supply within the dental pulp is a key step for the successful diagnosis and management of teeth involved in cystic lesions of the jaws. When anterior teeth are involved in cysts, vitality tests should be carried out on all teeth likely to become involved in the field of operation. Nonvital teeth should receive root canal treatment[13]. Erupted teeth related to a large developmental cyst or cystic lesions may remain vital even though the supporting bone has largely been lost. With infected cysts, there may be a temporary absence of a vital response in the adjacent teeth due to pressure interference with sensory transmission in the pulp[1]. Ischemia and degeneration of pulp tissue may be induced by the compression of the cystic lesion to the peripheral tissue of the root tip, which results in root resorption, decreased pulp vitality and even pulpal necrosis[41].

When a cyst involves the apices of one or more healthy teeth, the blood supply to the pulp may pass through the capsule of the lining. Stripping out the cyst wall will result in necrosis of the pulp of the teeth involved. Before surgery on a cyst that involves the roots of teeth, it is important to decide provisionally which teeth are to be conserved and which are useless and should be extracted[1]. It is also necessary to schedule regular follow-up appointments to monitor clinical signs and pulp vitality if the involved teeth are preserved without root canal therapy after the cyst has been enucleated.

Extraction of involved teeth

Extraction of nonvital teeth

A tooth associated with a periapical cyst usually suffers from a carious lesion or an injury, leading to the loss of pulp vitality. The surgical removal of periapical cysts has specific indications such as the failure of conservative endodontic treatment, a high risk of tooth fracture during access to the pulp canal, narrow and calcified pulp canals, a nonrestorable tooth or large cysts. For a large cyst, the surgical removal of the cyst can be associated with an apicoectomy or with the concomitant extraction of the associated tooth, depending on the viability of its maintenance[13,21]. A nonvital primary tooth associated with a cyst is removed from the mixed dentition.

Extraction of impacted tooth

A permanent premolar or incisor tooth in a dentigerous cyst is retained whenever possible. During the removal of the cystic lesion, the extraction of the unerupted permanent third molar, inverted impacted tooth or supernumerary malformed tooth is usually carried out[1,49,50].

Mandibular OKC and unicystic ameloblastoma are often associated with impacted third molars. Some reports have indicated that up to 80% of these lesions are associated with an unerupted mandibular third molar[51,52]. The standard treatment for these lesions is enucleation and extraction of the involved teeth, but the treatment plan is difficult to work out for huge cystic lesions with deeply impacted teeth. In these circumstances, enucleation along with simultaneously removing the impacted teeth may cause nerve injury or pathological mandibular fracture during surgery. Sun et al[34] found that after marsupialisation, all the cystic lesions shrunk and all the impacted teeth with or without mature roots moved towards the bony windows. The distances of tooth movement were from 8.3 to 12.1 mm, which facilitated tooth extractions during second-stage surgery (enucleation). After the secondary surgery, no numbness of the ipsilateral lower lip occurred. There were no mandibular fractures or other complications associated with this surgery modality[34]. When the third molar is deeply impacted within the cyst cavity, a combined orthodontic-surgical procedure may further facilitate tooth extraction and reduce the risk of damage to the inferior alveolar nerve and the possibility of pathological fractures[31,53].

Extraction of involved standing teeth

Some of the permanent teeth involved are extracted during cyst enucleation and marsupialisation, possibly because the teeth interfere with the complete removal of the cystic lesions or the teeth are severely loose. Dentigerous cysts rarely recur after enucleation even when the teeth involved are preserved[54]. However, the preservation of an involved tooth in the OKC may compromise proper enucleation of the lesion and increase the chance of recurrence when the tooth roots are involved in the OKC[22,24,40,55]. Therefore, the surgeon should consider extraction of the affected tooth in cases of root involvement by the lesion if there is any doubt that pathologic tissue may be left behind[55,56]. However, as OKC is more prevalent in younger patients, tooth extraction may not be a widely acceptable treatment for cosmetic reasons and due to possible occlusal complications. Naruse et al[40] suggested in their study that the patient should make the final decision about whether to preserve the tooth or not once the pros and cons have been explained. In some situations, patients preferred the risk of recurrence to losing vital teeth.

Although there have been some retrospective studies about the association between the type of surgical procedure and the rate of OKC recurrence[57,58], only the study by Naruse et al[40] specifically examined the correlation between tumour recurrence and the surgical modality when the tooth root was in contact with the margins of the primary tumour. The results of their study demonstrated that conservative treatment (32.4%) was significantly associated with OKC recurrence compared with radical treatment (extraction) (3.6%); therefore, teeth that remain in contact with primary tumours may present a risk for recurrence, as other authors have suggested[22].

Preservation of the involved teeth

Preservation of the involved teeth with/without root canal treatment

When a cyst is to be treated in a young patient with positive pulp vitality, different treatment options may also be considered to support tooth preservation; these options include marsupialisation followed by enucleation, enucleation without the treatment of the involved teeth, or enucleation with apicectomy of the involved teeth[19,39,40,59]. Marsupialisation can reduce damage to anatomical structures and may facilitate new bone formation to fill the defect, enabling the cavity to gradually decrease in size[39,60]. The radical treatment (extraction) of teeth that are in contact with lesions is a promising approach for preventing the recurrence of OKCs; however, as OKC is more prevalent in younger patients, tooth extraction may not be a widely acceptable treatment due to cosmetic concerns and occlusal complications. Therefore, a more elaborate peripheral osteotomy with a bone bur may be required when apicoectomy is selected[40].

Liao et al[59] evaluated the tooth vitality of teeth involved with OKC using the electric pulp vitality test during more than 6-months postoperative follow-up. There were 237 teeth involved in 42 patients with OKC, where root canal therapy was not received. Positive pulp vitality in the study group of marsupialisation in combination with secondary enucleation (71.56%) was significantly higher than that of simple enucleation

(36.72%) ($P < 0.01$). Pittl et al[61] present the case of a 49-year-old woman with a rare, large KCOT of the mandible extending from teeth 37 to 47. The cyst was enucleated by removing the surrounding bone. The cystic defect and the area surrounding the roots of the affected teeth were carefully swabbed with Carnoy's solution. Teeth interfering with the cystic lumen were preserved. Recurrence was observed 1 year later between teeth 43 and 45 and was treated by single enucleation with the use of Carnoy's solution. After the second surgery, teeth 35 to 45, which were interfering with the KCOT, still elicited a positive response to dental pulp testing with dry ice. As no other pathologies were detected, there was no need for endodontic treatment. No further signs of recurrence were observed after a total observation period of 7 years.

Timing and technique of root canal treatment

Root canal infection is the primary cause of periapical lesions. Therefore, if root infection is eliminated by nonsurgical root canal therapy, the lesions should heal. It is a general belief that large cyst-like periapical lesions caused by root canal infection are less likely to heal after nonsurgical root canal therapy. To achieve satisfactory periapical wound healing, surgical removal of periapical cysts must include the elimination of the root canal infection[62].

The causative tooth of an apical periodontal cyst is treated with dressing and root canal therapy either shortly before or during the surgery[13]. The root filling is usually carried out immediately prior to the surgical intervention; however, if it is not possible to dry the canal because the discharge from the cyst into the canal cannot be arrested, the root filling has to be inserted during the surgery[13]. If the root filling has not been done prior to the surgery, a retrograde root filling should be considered. In accordance with generally accepted practice, an attempt is made to retain the anterior teeth related to a periapical cyst whenever possible. Enucleation of the periapical cyst is usually followed by apicoectomy, retroinstrumentation, and retro-obturation with mineral trioxide aggregate[20]. Mineral trioxide aggregate (MTA) in endodontics has several desirable properties[63] and has consistently shown overgrowth of cementoid and osteoid tissues, with potential for periodontal fibre regeneration[64].

If healthy teeth are involved with developmental cysts or cystic lesions and root canal therapy is planned, root filling is usually completed before cyst enucleation.

Apicoectomy and crown-to-root ratio

Periapical surgery comprises a simple curettage of infected or inflamed tissue, removal of an infected or damaged root apex or a retrograde filling to avoid communication between the root canal system and the periapical tissue[65], or a combination of these. Enucleation of periapical cysts is routinely followed by apicoectomy[20]. Any apices of root-filled teeth protruding into the cavity are cut back to just below the inner surface of the lining[1]. The goal of cutting the root end is to eliminate the complex apical ramifications of the root canal system. Furthermore, apicectomy simplifies the debridement of the pathologic tissue, in particular at the lingual aspect of the root end, thus allowing for better control of haemostasis and improving visibility. An anatomic study of the root apex suggested that at least 3 mm of the root end must be removed to reduce 98% of the apical ramifications and 93% of the lateral canals[66]. Current recommendations of root-end resection suggest the removal of 3 mm[67].

Zhao et al[24] retrospectively analysed the clinical, radiological and histopathological features of 19 recurrent OKCs and found the recurrent lesion was involved with the roots of the teeth in three out of six cases where teeth were preserved. They thought recurrence might be due to incomplete removal of the epithelium around the tooth roots, which extended into the cyst cavity. The removal of the affected teeth or treating them with apicoectomy is recommended if the roots extend into the cyst lumen and interfere with the complete removal of the cyst wall. However, the majority of primary OKCs occur in the mandibular molar region; an apicoectomy against mandibular molars is often inaccurate because it is anatomically difficult to access compared with the anterior region[22].

As a consequence of root-end resection, the root-to-crown ratio (RCR) or crown-to-root ratio (CRR), respectively, is altered. Both ratios are referred to in the literature; studies about the anatomic root length (RL) preferably use the term RCR, whereas prosthodontic articles mostly use the term CRR. The CRR is one of the primary variables in the evaluation of the suitability of a tooth as an abutment for a fixed or removable partial denture[68]. A finite element analysis has evaluated the influence of root-end resection on the biomechanical response of a single-rooted tooth[69]. The study reported that apical root resection did not significantly alter stress distribution and tooth displacement until it reached 6 mm. The authors concluded that 3 mm of apical root resection appeared to be mechanically acceptable.

A study by von Arx et al[70] assessed the length of apicectomy and calculated the loss of RL and changes of RCR after apical surgery. In their prospective clinical study, CBCT scans were taken pre- and postoperatively. From these images, the crown and RLs of 61 roots (54 teeth in 47 patients) were measured before and after apical surgery. The mean length of root-end resection was 3.58 ± 1.43 mm (relative to the crestal bone level). This amounted to a loss of 33.2% of clinical and 26% of anatomic RL[70].

Micro-computed tomography (micro-CT) was applied to elucidate the relationship between the 3D root surface area (RSA) and the two-dimensional (2D) CRR of extracted teeth to classify the periodontitis and assign a periodontal/prosthetic prognosis[71]. A total of 31 maxillary and 35 mandibular single-rooted human premolars were examined. The amount of periodontal support on the basis of 3D RSA and 2D RL at CRRs of 1:1, 5:4, 3:2 and 2:1 were analysed. The coronal 21% to 22% 2D RL and the 26% to 28% 3D RSA bone loss apical to the cementoenamel junction corresponded to a CRR of 1:1, correlating with mild-moderate periodontitis. The coronal 30% to 31% 2D RL and the 41% to 42% 3D RSA bone loss corresponded to a CRR of 5:4, correlating with severe periodontitis[72]. More severe clinical attachment loss (CAL) was observed in the 3D RSA measurement than in the 2D RL measurement at the evaluated CRRs.

Although root canal therapy is an effective treatment for mature teeth, with a favorable prognosis, devitalised teeth are more vulnerable and prone to being lost later in life[73]. Furthermore, an apicoectomy may change the CRR or periodontal support, and the mandibular molar apicectomy can possibly be followed by impaired sensation in the lower lip. Thus, the preservation of teeth with pulp vitality is of clinical significance when cystic lesions of the jaws involve standing teeth and are to be treated surgically.

Management of impacted teeth in a cyst cavity

Extraction of teeth

The vast majority of dentigerous cysts are associated with impacted mandibular third molars, followed by the permanent maxillary canines and the maxillary third molars[4]. However, in a review by Al Tuwirqi et al[21], the substantial majority of dentigeous cysts involve the mandibular second premolar and the mandibular second molar, followed by the maxillary permanent canines and rarely the mandibular incisors.

The impacted third molar or supernumerary tooth in dentigerous cysts or other cystic lesions is generally removed during cyst enucleation. The premolar or the anterior teeth enclosed in the cyst, especially of children, will be preserved by marsupialisation. An inverted permanent tooth or a deeply impacted tooth is often difficult to manage. Celebi et al[53] treated the dentigerous cyst that arose from a deeply impacted mandibular third molar with orthodontic extraction combined with marsupialisation therapy. This orthodontic-surgical procedure reduced the risk of nerve damage and pathological fracture of the mandible.

Lim et al[74] reported a case of an 18-year-old man who had an impacted premolar accompanied with a large dentigerous cyst. The tooth was extracted surgically and transplanted to an edentulous alveolar ridge. Root canal treatment was performed 3 weeks after the surgery. The transplanted tooth was functional without any pathologic signs. This protocol provides a viable option for saving an impacted tooth in the case of cyst enucleation.

Coronectomy with enucleation of cyst

Dentigerous cysts develop from the follicles of teeth that have failed to erupt and thus are most frequently associated with impacted mandibular third molars. If the cyst is associated with mandibular teeth, this can complicate surgery, with the risk of inferior alveolar nerve injury due to the removal of either the cyst or the unerupted tooth where proximity to the inferior alveolar nerve is present. Coronectomy is an elective procedure that is indicated in such cases. It involves careful removal of the crown of the tooth while maintaining the roots[75].

Despite the increase in popularity of coronectomy as an adequate preventative technique for inferior alveolar nerve protection, its use in conjunction with the management of dentigerous cysts has not been widely reported in the literature. O'Riordan[76] described a Gorlin-Goltz patient who had undergone coronectomy and the removal of an OKC of the mandibular left second premolar. Malden and D'Costa e Rego[77] first reported the use of coronectomy with a dentigerous cyst. Most recently, Patel et al[78] presented a case series of 21 patients with dentigerous cysts and coronectomy. The performance of coronectomy for dentigerous cysts is based on the principle that the cyst originates from the enamel-dentine junction. Therefore, removing the crown below this junction completely removes the cyst at its source[77,78].

A retrospective review of 68 patients was undertaken by Henien et al[35] in a single department where 73 teeth with associated dentigerous cysts were treated by coronectomy. Their results show that one patient experienced permanent injury of the inferior alveolar nerve. There were no intraoperative mandibular fractures in this case series. Four coronectomy roots required retrieval at 2, 4 and 20 months and 10 years after the initial surgery due to persistent surgical site infection and incomplete coronectomy with retained enamel and associated cystic tissue leading to symptoms. The authors suggested that coronectomy, in conjunction with enucleation of the dentigerous cysts, is an effective treatment when there is concern about inferior alveolar nerve injury or jaw fracture from extraction, with minimal morbidity seen in both the short and long term.

Marsupialisation and decompression

Marsupialisation and decompression are very similar surgical procedures aimed at decreasing the cystic size by reducing the pressure of the cystic fluid and inducing bony apposition to the cystic walls[79]. However, technically they have different meanings.

Marsupialisation of cysts of the jaws with retention of part of the lining, advocated by Partsch in 1892[1], creates a larger communication or pouch connecting the oral and cystic cavities after unroofing the outer wall of the cyst and suturing the cyst wall to the oral mucosa[80,81]. It has become known as the Partsch I technique. An obturator (cyst plug or acrylic stent) is fabricated and placed 1 week later, which must be progressively modified to fit into the cavity as the cyst heals[15,81,82]. The second procedure (enucleation) is often carried out in cases of OKC and unicystic ameloblastoma to eliminate the residual lesion 3 to 6 months later[83,84]. Decompression, proposed by Thoma in 1958[85], requires a small-diameter polyethylene or rubber drainage tube that is sutured *in situ* or attached to an adjacent tooth or to orthodontic brackets with a stainless steel ligature wire, creating a smaller opening or connection between the cyst and the oral environment until an epithelial slit forms[86-88]. The decompression procedure may be easier to perform and more conservative than marsupialisation, sparing more soft and hard tissue, and is particularly indicated in children[7,89]. Marsupialisation may be considered a resolutive treatment, not to be followed by enucleation, whereas decompression alone without subsequent enucleation is rarely indicated[90]. Controversy exists about whether marsupialisation/decompression should be considered a resolutive treatment or whether it should be followed by enucleation[87,91,92].

When preservation of the impacted teeth is planned, marsupialisation is a rather conservative treatment option[27], with the advantage of promoting spontaneous eruption of the involved tooth within the cyst[16]. However, this technique has some disadvantages[1,21]; the two-stage surgical procedure may be intolerable for a child and leave behind pathological tissue and, in a large cystic cavity, it may take a long time for the bone to regenerate.

Two research papers found that between 71.4% and 72.4% of the individuals who participated in this study presented with natural eruption of the teeth enclosed in the cyst after marsupialisation had been performed[16,29]. The key factors in the eruption of a tooth in the arch are the status of root development and the angle and depth of the tooth in the jaw. Together with incomplete root development, the impacted teeth show potential for eruption if the angle is less than 25 degrees and the space between adjacent teeth is greater than the size of the teeth[91]. It is well established that the average time it takes teeth to erupt without carrying out orthodontic traction is approximately 3 months[16,29].

The impacted tooth without complete root formation or with an open apex had considerable potential to erupt after marsupialisation[92]. If the dental root has matured, the tooth might not erupt to the normal position after marsupialisation[29,33,93]. Patients aged over 10 years would not be expected to have spontaneous eruption of an impacted tooth, indicating the need for orthodontic treatment to guide occlusion or surgical removal of the entire cyst with the impacted tooth[91].

Potential pulp revascularisation after cyst enucleation/apicectomy

Bone cavity healing following cyst enucleation

Osteogenesis of a bone defect in the jaws begins with the formation of a blood clot, which is later replaced by osteogenic granulation tissue[83]. In the healing phase, vascular changes are the most important feature, and conventional radiographs cannot reveal these changes in the bone. Zainedeen et al[94] measured blood-flow velocity around the radiolucent lesions by colour Doppler before surgery and at 1 week and 6 months after surgery to assess the reliability of ultrasonography as a tool for monitoring the healing of jaw lesions. They found that the average blood-flow velocity increased 1 week after surgery (5.84 cm/s) compared with the velocity before surgery (4 cm/s) ($P < 0.05$). The formation of a vascular network at the same time as the formation of new bone is extremely important; this network is vital for cellular viability. Another important function of this network is the transport of progenitor cells, and several cytokines and growth factors are required for balanced bone regeneration. The angiogenesis and osteogenesis processes at the defect site are interconnected in a structural, biochemical and functional way[95].

In most cases, bone defect after enucleation is completely surrounded by solid bone walls apart from the site of approach. This facilitates a stable blood clot leading to a regular and safe healing process. With the increasing size of the cyst, the risk of wound infection rises due to retraction of the blood clot from the cyst wall. A blood clot in the bone cavity has a similar function to a hematoma at the fracture site. Pluripotent hematomas were thought to serve not only as an initial fibrin scaffold within which mesenchymal stem cells could perform their functions, but also as a temporary 'reservoir' for the continuous release of pleiotropic growth factors responsible for bone regrowth[96]. During the first 4 weeks, angiogenic and osteogenic cells originating from the adjacent bone walls and the periosteum turn a blood clot into granulation tissue and woven bone towards the centre of the defect. The process of bone healing is stimulated by various cytokines, growth factors (eg, platelet-derived growth factor [PDGF], insulin-like growth factor [IGF], fibroblast growth factor [FGF], transforming growth factor beta [TGF-b], bone morphogenetic protein [BMP]) and stem cells[97,98].

Pulp revascularisation after pulp regeneration treatment and tooth transplantation

The term 'revascularisation' originated from the dental trauma literature. In some cases, a tooth with incomplete root formation may be able to reestablish blood supply after autotransplantation or replantation[99,100]. Meanwhile, revascularisation procedures in pulp regenerative treatment involve root canal disinfection and blood clot induction[101,102]. Several case reports have shown successful clinical results (eg, an increase in RL and root thickness and apical narrowing)[103,104]. However, some have reported unfavourable outcomes[105].

The pulp is a highly vascularised tissue situated in an inextensible environment surrounded by rigid dentine walls, with the apical foramina being the only access. Whereas the pulp vascular system is established by vasculogenesis during embryonic development, angiogenesis (the sprouting of new vessels from existing ones) is the predominant process during pulp regeneration and therapeutic processes[36]. The driving force of angiogenesis is hypoxia[37], which can arise in situations where the pulp tissue is subjected to a disruption of oxygen supply such as in pathologic situations during carious/traumatic pulp injuries and during therapeutic procedures, including tissue regeneration and tooth transplantation. In all these situations, hypoxic cells secrete proangiogenic factors that induce sprouting angiogenesis or vasculogenesis, leading to vascular network formation in developing, engineered and regenerating tissues. Dental pulp cells under hypoxic stress release proangiogenic factors, with vascular endothelial growth factor (VEGF) being one of the most potent. Interestingly, dental pulp stem cells (DPSCs) have an important role in pulp revascularisation. Indeed, recent studies have shown that the DPSC secretome possesses angiogenic potential that actively contributes to the angiogenic process by guiding endothelial cells and even by differentiating themselves into the endothelial lineage[106].

Hypoxia as the driving force of angiogenesis in injured dental pulp tissue has been well established[37]. Under hypoxic conditions, DPSCs rapidly increase their expression of hypoxia-inducible factor 1 (HIF-1). HIF-1 mediates increased transcription of various angiogenic genes such as VEGF, PDGF AB, placental growth factor and angiopoietins. It also regulates the expression of angiogenic chemokines such as stromal cell-derived factor 1, sphingosine-1-phosphate and their receptors[107,108]. Hypoxia is thus a major regulator of angiogenesis, particularly by stimulating the paracrine angiogenic activity of DPCSs.

Vascular network formation in cocultures of DPSCs and human umbilical vein endothelial cells confirmed the paracrine angiogenic activity of DPSCs[109,110], which could be attributed to increased VEGF secretion and associated VEGF receptor 2 (VEGFR-2) signalling in the endothelial cells. DPSCs showing the ability to differentiate into endothelial-like cells *in vivo* and *in vitro* expressed the VEGFR-2 receptor[111,112]. Recently, evidence has shown that DPSCs are capable of *de novo* blood vessel formation, similar to embryonic vasculogenesis, by differentiating into vascular endothelial cells[106]. It can therefore be hypothesised that DPSCs residing in perivascular regions differentiate into endothelial-like cells and initiate the sprouting of new blood vessels from adjacent ones.

Tooth transplantations have a long clinical history and are mainly used for the replantation of avulsed teeth and during orthodontic treatments. In a nutshell, three approaches can be discerned: transplantation of 1) an immature tooth with pulp tissue, 2) an apicoectomised mature tooth, and 3) a tooth with removed pulp tissue[36]. Ideally, pulp tissue functionality should be conserved after transplantation, which implies the presence of a functional vascular network. In the first two approaches, it is believed that the vasculature of the transplanted tooth pulp tissue needs to be connected with the general blood supply for tissue survival. However, in an *in vivo* study in dogs, anastomosis between pre-existing vessels of transplanted pulp tissue and ingrowing blood vessels was seen in only a few teeth. Revascularisation of the pulp tissue was primarily the result of the ingrowth of newly formed vessels[113].

Potential pulp revascularisation after cyst enucleation/ apicectomy

A cyst or cystic lesion often extends to the apices of adjacent teeth, so that the removal of the capsule would involve the risk of injuring the nerve and blood supply of these teeth with a consequent pulp necrosis. In any cases of doubt, the vitality of such teeth should be checked over a prolonged period of time, but every effort should be made to safeguard the vitality of teeth as far as possible. The value of a tooth is much reduced if devitalised[13].

The response of dental pulp to trauma can be varied. Some pulp remains apparently normal with no adverse effects whereas other pulp becomes necrotic. Pulpal necrosis is a frequent sequel of trauma and will result in the development of a periapical lesion if microbial infection occurs. Conventional root canal treatment aims primarily to eliminate these bacteria as completely as possible[114,115]. Clinical evidence has shown that no pulpal infection followed enucleation in some cases where teeth were involved by developmental odontogenic cystic lesions and had not received root canal therapy[40,59]. However, it is not clear which factors contribute to pulp revascularisation – whether it is the age of the patient, the apical diameter of the involved tooth or the type of cystic lesion.

The apical size necessary for optimal pulp revascularisation has constantly been a matter of great controversy. A review by Fang et al[116] evaluated whether the apical diameter of teeth with necrotic pulp affects the outcomes of regenerative endodontic treatment and the minimal apical size needed to obtain proper pulp revascularisation. The apical diameters of the teeth were divided into three groups: a narrow-sized group (group N), < 0.5 mm (n = 10); a medium-sized group (group M), 0.5 to 1.0 mm (n = 25); and a wide-sized group (group W), > 1.0 mm (n = 60). The clinical success rates were 90%, 95.65% and 92.98% in groups N, M and W, respectively. These authors concluded that pulp revascularisation even for the teeth with apical diameters of < 1.0 mm can be achieved with a high chance of clinical success after regenerative endodontic treatment[116].

The results of a study by Marques-Ferreira et al[117] indicate that the shorter the root of transplants (L < 8.07 mm) and the longer the diameter of the foramen (> 1 mm), the greater the possibility of pulp revascularisation. When clinical signs and radiographic indicators of pulp or periapical pathology appeared, endodontic therapy was performed, which occurred in 39% of the transplants. On the other hand, it was only necessary to perform endodontic therapy on 8% of teeth with an open apex.

No publications were found on pulp regeneration or revascularisation after cyst enucleation, although some autotransplanted teeth with complete root formation that do not undergo root canal treatment could have the potential for revascularisation[118]. A vascular supply will be destroyed or pulp necrosis will occur during cyst enucleation or apicectomy. A vascular network already present in a standing tooth may connect with the newly formed vasculature in bone cavity, or the necrotic pulp tissues will be revascularised by the newly formed vasculature via the apex. Laser Doppler flowmetry is a well-established modality used to assess vascular flow in the dental pulp because of the ability of the laser beam to penetrate hard tissue[119]. The use of colour/ power Doppler US has been reported in the literature in evaluations of pathologic lesions and the monitoring of treatment[120,121]. It may be used for the monitoring of bone healing and pulp revascularisation after cyst enucleation or apicectomy[118,119,122].

Root canal treatment is an effective treatment for mature teeth, with a favorable prognosis. However, a tooth without vital pulp loses its defensive ability and becomes increasingly vulnerable to external forces. This decreased protection is often followed by tooth fracture and, ultimately, tooth extraction. The preservation of a tooth with pulp vitality should have important clinical significance when teeth are involved by cystic lesions in need of surgical management. Although there is considerable insight into the complex orchestrated angiogenic process in the dental pulp, many questions remain relating to the signalling pathways, timing of pulp revascularisation after cyst enucleation and influence of various conditions such as the size of bone cavity, size of apical diameter of involved teeth and the age of the patient. Further research is needed to elucidate these interesting areas.

Conflicts of interest

The authors reported no conflicts of interest related to this study.

Author contribution

Drs Yi ZHAO and Bing LIU contributed to the literature research and writing of the manuscript; Prof Yi Fang ZHAO contributed to the project design and the revision of the manuscript.

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