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Enucleation with or without adjuvant therapy versus marsupialization with or without secondary enucleation in the treatment of keratocystic odontogenic tumors: A systematic review and meta-analysis

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ABSTRACT

The purpose of this study was to compare the recurrence rate (RR) of keratocystic odontogenic tumors (KOTs) in patients who underwent enucleation with or without adjuvant therapy, to patients who underwent decompression with or without residual cystectomy. An extensive search of major databases through PubMed, EMBASE, and Cochrane CENTRAL was conducted to identify all relevant articles published without date and language restrictions from inception to December 2015. Relevant articles were selected based on the specific inclusion criteria. A weighted RR and odds ratio (OR) using a Mantel-Haenszel (M-H) test and random effect model with 95% confidence interval (CI) were performed. Meta-regression analysis was conducted to further identify the influence of the duration of follow-up periods on the overall OR. A total of 997 KOTs enrolled in 14 studies were included in this analysis. There was a significant advantage for the enucleation ± adjuvant therapy group in preventing recurrence for patients with KOTs (M-H, OR, 0.514; 95% CI, 0.302–0.875; p = 0.014). The overall pooled weighted RR for enucleation ± adjuvant therapy and decompression ± secondary cystectomy were 18.2% and 27.1%, respectively. The meta-regression analysis showed that duration of follow-up time did not significantly influence the OR of KOT recurrence (Q = 0.506, p = 0.646). In conclusion, initial cystectomy ± adjuvant therapy was associated with fewer recurrences than decompression ± secondary cystectomy.

1. Introduction

The keratocystic odontogenic tumor (KOT), formerly known as the odontogenic keratocyst (OKC), is of odontogenic origin. Unlike odontogenic cysts, the KOT shows locally aggressive behavior, has a high recurrence rate, and has a distinct and characteristic histologic appearance that caused the World Health Organization (WHO) in 2005 to reclassify this lesion as a tumor instead of a cyst (Barnes et al., 2005; Kramer et al.,1992; Brannon, 1976).

Radiographically, displacement of impacted or erupted teeth, root resorption, root displacement, or extrusion of erupted teeth may be evident (Brannon, 1976). KOTs may occur in any part of the jaws; however, in common with ameloblastomas, calcifying epithelial odontogenic tumors, and myxomas, it has a predilection for the posterior body of the mandible and ascending ramus. KOTs have a peak incidence in patients between the ages of 10 and 30 years and a slight male predominance (Myoung et al., 2001; Maurette et al., 2006; Zhou et al., 2005). KOTs are of great interest among oral and maxillofacial surgeons because of their high recurrence rate. The current literature has reported a recurrence rate of 0%–50% (Johnson et al., 2013). Like other odontogenic tumors, the KOT has a tendency to expand through bony walls and to invade deeper structures (Tolstunov and Treasure, 2008).

Various treatment modalities have been used in the treatment of KOTs and can be classified as aggressive or conservative approaches. Aggressive approaches could be simple enucleation

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without adjuvant therapy or enucleation with adjuvant therapy, such as the application of Carnoy's solution, cryotherapy, or peripheral ostectomy. Conservative approaches include decompression with or without subsequent residual cystectomy.

The treatment of KOTs remains controversial, and there is no consensus as to whether an aggressive treatment is superior to conservative treatment in reducing the recurrence rate for treatment of patients with KOTs. Therefore, the authors of the present study tested, through a meta-analysis, the null hypothesis that for management of patients with KOTs there is no difference between these treatments The specific aim of this study was to compare the recurrence rate of KOTs in patients who underwent enucleation with or without adjuvant therapies to patients who underwent decompression with or without residual cystectomy.

2. Materials and methods

To ensure a systematic approach and more reliable findings, this systematic review was conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement for reporting systematic reviews (Liberati et al., 2009).

2.1. Literature search strategy

An extensive electronic search without date or language was conducted from the respective dates of inception to December 2015 using the following online databases, with specific keywords according to PICOS criteria: PubMed, Ovid MEDLINE, and Cochrane CENTRAL. The electronic search and the PICO strategy are shown in Table 1. The search combination of all keywords of PICOS component was (keratocystic odontogenic tumor) OR odontogenic keratocyst) OR KOT) OR okc OR kot) AND decompression) OR marsupialization) OR decompression followed by enucleation) OR compression followed by residual cystectomy) OR cystostomy) exteriorization) OR fenestration) OR pouch procedure) OR Partsch operation) OR marsupialization followed by secondary cystectomy) AND enucleation) OR enucleation with adjuvant therapy) OR enucleation with curettage) OR enucleation plus Carnoy's solution) OR enucleation with cryotherapy) OR enucleation with peripheral ostectomy) AND recurrence) AND relapse).

Table 1
Search strategy for the systematic review.

Problem	Keratocystic odontogenic tumors OR kcot OR kot OR odontogenic keratocyst OR okc OR nonsyndromic keratocystics odontogenic tumuors.
Intervention	Decompression OR marsupialization OR decompression followed by enucleation OR compression followed by residual cystectomy OR cystostomy OR marsupialization followed by secondary cystectomy OR exteriorization OR fenestration OR pouch procedure OR Partsch operation.
Comparisons	Simple enucleation OR enucleation with adjuvant therapy OR enucleation with curettage OR enucleation plus carnoy s solution OR enucleation with cryotherapy OR enucleation with peripheral ostectomy OR enucleation with liquid nitrogen cryotherapy OR enucleation with chemical cauterization.
Outcomes	Recurrence OR relapse.
Study design	Randomized controlled trials OR controlled clinical trials OR comparative studies OR case series.
Search combination	Populations AND intervention AND comparator AND outcome AND study design.
Language	No restriction.
Electronic data base	MEDLINE/PubMed and Cochrane Central Register of Controlled Trials (CENTRAL)/EMBASE
Focused question	For patients with keratocystic odontogenic tumors, dose enucleation ± adjuvant therapy produce fewer recurrent KOT when compared to decompression ± residual cystectomy?

MeSH, medical subject heading adjuvant.

To avoid missing any articles, the references of each selected publication that yielded from an electronic search were performed by Google Scholar and by hand.

2.2. Study eligibility

2.2.1. Inclusion criteria

Inclusion criteria were adopted using the following PICOTS components. Population (P): adult, young and elderly patients with nonsyndromic, parakeratinized odontogenic tumors (virgin or recurrent) that were diagnosed and confirmed histologically. Intervention (I): Marsupialization or decompression with or without secondary cystectomy and adjunctive therapy. Comparator (C): Enucleation with or without adjunctive therapy, such as cryotherapy, peripheral ostectomy, or Carnoy's solution. Outcome (O): Recurrence rate of KOT for the two universally accepted treatments. Time (T): Adequate follow-up period. Study Design (S): Prospective randomized controlled clinical trials, controlled clinical studies either prospective or retrospective, retrospective reviews, and case series comparing enucleation with or without adjuvant therapy to decompression with or without secondary cystectomy with regard to recurrence rate with an adequate follow-up period.

2.2.2. Exclusion criteria

The following exclusion criteria were used: animal or *in vitro* studies; editorial letters; articles in which a total number of treated KOT was less than 10; articles that did not sufficiently specify a type of surgical method; articles that included patients with nevoid basal cell carcinoma syndrome (NBCCS or Gorlin-Goltz syndrome), as there can be newly developed cysts in these patients, resulting in bias when estimating recurrence rate, except for studies that specified and accounted for patients with NBCCS separately (Blanas et al., 2000; Antonoglou et al., 2014); studies that did not give an adequate follow-up period; and reviews articles.

2.3. Data extraction process

The screening process of articles and eligibility of retrieved articles were reviewed by two independent reviewers. Any disagreement between the two reviewers was resolved by a third judge. The following data were extracted from the studies: authors, year of publication, study, male-to-female ratio, patient age (average), number of patients/lesions, location of lesion (maxilla or mandible), association with unerupted tooth, surgical treatments, follow-up period, and recurrence rate.

2.4. Critical appraisal of individual studies

Two authors (E.E and M.A) independently assessed the risk of bias for each study by using the Newcastle–Ottawa Scale (Wells et al., 2013). Disagreements were resolved by discussion or by involving the third author (E.A) to adjudicate. A study could receive a maximum of one star for each numbered item within the selection and outcome categories. A maximum of two stars could be given for comparability. The greatest score that could be given to a study according to the Newcastle–Ottawa Scale was nine stars (low risk of bias). Studies scoring six stars or more were considered to be of high quality.