

Systematic Review Clinical Pathology

Recurrence rate following treatment for primary multicystic ameloblastoma: systematic review and meta-analysis

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Abstract. Opinions regarding the treatment of multicystic ameloblastoma are divergent due to its benign nature and the high rate of recurrence if not adequately excised. The aim of the present study was to perform a systematic review of the literature for a qualitative and quantitative assessment of studies addressing primary multicystic ameloblastoma with regard to treatment and recurrence. Searches were conducted of the Ovid Medline and Embase databases for articles published up to January 2014. Based on predefined eligibility criteria, studies were selected in a two-stage screening process conducted by two independent reviewers. Quality assessment of the selected articles was performed using the modified criteria of the Agency for Healthcare Research and Quality. The meta-analysis was performed using Review Manager (RevMan) software. Statistical heterogeneity was investigated by performing a χ^2 test at the 5% significance level (P < 0.05) and determining I^2 . The relative risk of recurrence was 3.15-fold greater (95% confidence interval 1.98-5.00) when conservative treatment was performed on primary multicystic ameloblastoma in comparison to radical treatment (P < 0.00001) for treatment effect; $I^2 = 0\%$ and P = 0.48 for heterogeneity). The findings justify the treatment of primary multicystic ameloblastoma with bone resection.

Key words: ameloblastoma; recurrence; review; meta-analysis.

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Ameloblastoma was originally described by Cuzack in 1827 and subsequently detailed by Broca in 1868. The World Health Organization (WHO) classifies ameloblastoma as a tumour formed by odontogenic epithelium with mature fibrous stroma without an odontogenic ectomesenchyme. Ameloblastoma accounts for 1% of tumours that affect the oral-maxillofacial complex and 13–58% of odontogenic tumours, and is classified into four types based on clinical, histological, and

radiographic findings: unicystic, multicystic, peripheral, and desmoplastic. Each type has a distinct clinical behaviour and requires different forms of treatment.

Multicystic ameloblastoma is considered the most common variant and

consists of a locally aggressive tumour that mainly affects the body and posterior portion of the mandible in patients in the third and fourth decades of life^{3,8,9}: there is no predilection for the male or female sex. 10-13 The diagnosis is generally made through a combination of imaging examinations (X-ray and computed tomography) and biopsy to determine the histological type. 12 In an X-ray, the tumour exhibits a well-defined unilocular or multilocular osteolytic image surrounded by a radiopaque margin, often with expansion of the bone cortex, with the possibility of root resorption 13 and occasional association with an impacted tooth. 12

Treatment is classified as conservative or radical. Conservative treatment includes enucleation, curettage, and surgical excision with peripheral osteotomy or other adjuvant therapy, such as cryotherapy or Carnoy's solution. Radical treatment consists of bone resection. In the mandible, resection can be completed through segmental osteotomy or a mandibulectomy, or can be marginal (when the lower border is preserved, thereby maintaining bone continuity). In the maxilla, radical treatment comprises maxillectomy, which is classified as partial or total based on the extent of the resection. ¹⁵

Surgical treatment of the multicystic variant remains a controversial issue, as the tumour has a high rate of recurrence if not adequately excised, but the metastatic potential is low. 15 With conservative treatment, 55-90% of cases recur, whereas the recurrence rate with more radical treatment is 15-25%; however, in the latter case, the patient experiences serious aesthetic and functional impairment as well as the need for reconstructive surgery. 16 Nakamura et al. found recurrence rates of 7.1% following radical surgery and 33.3% following conservative surgery, which are much lower rates than those reported in other studies, encouraging the use of more conservative treatment. Similarly, Hasegawa et al. reported a recurrence rate of 43.5% following conservative treatment. 18

Hong et al. concluded that treatment tends to be radical. ¹⁹ When age and location are the same, going from conservative treatment to resection with a bone margin, or going from the latter to segmental resection or maxillectomy, the recurrence rate is diminished by 20%. The authors also stated that tumours with a multicystic radiographic appearance have a 3.02-fold greater chance of recurring in comparison to those with a unicystic appearance and that patients with only bone expansion without rupture of the cortex have a lower

chance of recurrence in comparison to those with rupture of the bone cortex.

Due to its benign nature and slow growth, many surgeons believe that the treatment of ameloblastoma should initially be conservative, with radical surgery only performed when necessary after a recurrence. In other words, the diagnosis of a multicystic ameloblastoma should not necessarily indicate immediate bone resection, and treatment should be performed with the complete removal of the tumour while preserving the lower portion of the mandible whenever possible.²⁰

Considering the divergent opinions on the treatment of multicystic ameloblastoma, the aim of the present study was to perform a systematic review of the literature for a qualitative and quantitative assessment of studies addressing primary multicystic ameloblastoma with regard to treatment and recurrence.

Materials and methods

Focused question

The following question guided this study: What form of treatment for primary multicystic ameloblastoma results in the lowest rate of recurrence?

Search strategy

Searches were performed of the Ovid Medline and Embase databases for articles published up to January 2014. The search strategy involved combinations of medical subject heading (MeSH) terms and key words for the Ovid Medline database and the appropriate modifications for the Embase database. The search strategy was as follows: (1) Population: "Ameloblastoma" OR "Jaw neoplasms" OR "Mandibular disease" OR "Maxillary disease" OR "Ameloblastoma\$" OR "{(jaw or mandibular or maxillary) and neoplasm\$}" OR "{(jaw or mandibular or maxillary) and disease\$}" OR "{(jaw or mandibular or maxillary) and tumo\$}" OR "(odontogenic and tumo\$)". (2) Intervention: "Curettage" OR "Decompression, surgical" OR "Decompres-"Chloroform" sion" OR OR "Ethanol" OR "Acetic acid" OR "Cryosurgery" OR "Cryotherapy" OR "Curettage\$" OR "Decompression\$" OR "{(carnoy or carnoy's) and solution\$}" OR "Cryotherap\$" OR "Cryosurg\$" OR "Enucleation\$" OR "{(mandibular or jaw or maxillary or marginal or box or wide or radical or conservative) and resection\$}" OR "Mandibulectomy" OR "Maxillectomy" OR "(peripheral and osteotomy)" OR "(liquid and nitrogen)" OR "{surgical and (treatment or management)}" OR "{(radical or conservative) and surger\$}" OR "Excision\$" OR "Marsupialization\$". (3) Outcomes: "Neoplasm recurrence, local" OR "Retreatment" OR "Treatment outcome" OR "Morbidity" OR "Recur\$" OR "Relapse\$" OR "(long and term and effect\$)" OR "Morbidit\$" OR "Retreatment\$" OR "(effective and therap\$)" OR "(Treatment\$ and outcome)" OR "(Follow and up)".

The key words were then combined in the following way: Population AND Intervention AND Outcomes.

Manual searches of the reference lists of the articles were also performed to find further studies that were not included in the electronic databases.

Outcome measure

The primary outcome of the study was the recurrence rate.

Eligibility criteria

The inclusion criteria were articles addressing the treatment of primary multicystic ameloblastoma and level of evidence up to the fourth level, as established by the Oxford Centre for Evidence-Based Medicine.21 The exclusion criteria were treatment for ameloblastomas in uncommon locations, articles that referred only to the desmoplastic histological type, articles that referred only to one type of treatment, articles that referred only to the treatment of giant ameloblastomas, cases series with fewer than 10 cases, mean postoperative follow-up period of less than 5 years or not specified, treatment only for individuals less than 20 years of age (due to the tendency towards conservative treatment in this age group), use of histological classification different from that recommended by the WHO, failure to describe the histopathological analysis, failure to distinguish unicystic and multicystic tumours from the histological standpoint regarding the treatment employed, failure to specify treatment, failure to describe recurrences, and study with the same population as that of another study included.

Screening methods

The article selection process was conducted in two steps by two independent researchers (R.A.C.A. and J.C.B.) who were initially blinded to each other's results. After a comparison of the findings, disagreements regarding the inclusion or

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