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Review

Recurrence rate of odontogenic myxoma after different treatments: a systematic review

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Abstract

Our aim was to establish the recurrence rate of odontogenic myxoma after different treatments. Our search covered papers from 1972-2017 from different sources. The papers were evaluated and critically appraised by two independent investigators. The recurrence rate and 95% CI were calculated in relation to each specific treatment, and the chi squared test was calculated to find out if there was any significant difference in the recurrence rate between conservative treatment and resection. The overall recurrence rate was 5 of 39 patients (13%) during a mean follow up period of 10 years. With conservative treatment the recurrence rate was 4/22 (19%) (mean follow up 11 years) and after resection it was 1/17 (6%) (mean follow up nine years). Maxillary lesions were more likely to recur than mandibular ones. Quality of life variables such as disfigurement and neural deficit were more common after resection than with conservative treatment. The frequency of recurrence was relatively low over 10 years' follow up, irrespective of whether resection or a more conservative approach was used, despite being slightly lower (as might be expected) after resection. Conservative treatment should be considered first to avoid resection-associated morbidity and the effect on the quality of life. Maxillary lesions have more room to spread before they are clinically evident, making them difficult to treat optimally and contributing to the recurrence rate.
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Keywords: odontogenic myxoma; odontogenic tumors; recurrence; surgical management

Introduction

Odontogenic myxoma is an uncommon benign odontogenic tumour that derives from mesenchyme, or odontogenic ectomesenchyme, or both, with or without epithelium.[1] It comprises 0.5% of all bony tumours and 3%-6% of odontogenic tumours.[2] According to some studies it is the second most-common benign odontogenic tumour,[3] is commonly seen in the mandibular premolar-molar region, and favours the female sex. It affects all age groups but is commonly seen in the second to fourth decades of life. Radiographically unilocular radiolucency, multilocular radiolucency, and mixed radiolucency and radio-opacity have been reported. Various treatments have been tried, ranging from conservative enucleation to radical resection.

The tumour is associated with a high recurrence rate ranging from 10%[4] to 43%[5] with a mean of 25%,[6] and this is attributed to its myxomatous nature, lack of a capsule, and

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penetration of the lesion into the surrounding bone without its immediate destruction.[7] The margins are not clearly identifiable radiographically, possibly because of the lack of immediate destruction that leads to incomplete removal and finally to recurrence. The high recurrence rate has mostly been established in case reports.

Curative treatment has not been properly standardised, probably because of the rarity of the tumour, so substantial single-centre prospective studies are not possible.[4] Because of insufficient, standardised, evidence-based surgical guidelines, its therapeutic management is difficult. The rationale of this review was therefore to appraise critically the available published evidence about the recurrence rates of odontogenic myxoma and its management.

Material and methods

The conduct of this review followed the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA).[8] The International Prospective Register of Systematic Reviews (PROSPERO) was searched by entering titles and keywords, and no existing record of registration was found. The PROSPERO registration number for this review is CRD42018098899.

Eligibility criteria

We included papers that belonged in one of the following levels of evidence: structured reviews of randomised controlled trials; meta-analyses of randomised controlled trials; randomised controlled trials; structured review of meta-analyses of controlled clinical trials; controlled clinical trials; structured reviews or meta-analyses of case series; prospective case series; or retrospective case series. We also included papers that had specified treatment and its correlation with recurrent and non-recurrent cases, and histopathologically confirmed cases. All papers had to be published in English.

Our exclusion criteria were: papers about soft tissue odontogenic myxoma; papers that had only a specific group of subjects (such as any particular age group or sex); papers restricted to a particular jaw or particular site on the jaw; and animal studies.

Sources of information, and search

We made an extensive search of each electronic database; PubMed (Medline), Cochrane Database of structured reviews (evidence-based medicine), SCOPUS, LILACS virtual health library, ISI Journal Citation Reports, Ovid Multi-database and Access Science for articles from 1January 1972 to 31 December 2017. Keywords used were: (odontogenic AND myxoma AND tumor) AND (recur OR relapse OR recurrence OR surgical management).

Selection of studies

Papers were selected in three stages (search, evaluation, and critical appraisal) by two investigators (MS and SNG) independently, and neither was aware of the other's decision. If there was any controversy it was settled by a joint decision, and if they could not reach a consensus, then the opinion of the third investigator (KS) was considered final.

In the first round (search) all abstracts related to recurrence and surgical treatment were assessed by the two investigators independently. Full texts were obtained for all relevant articles.

In the second round (evaluation) the full text of each paper was reviewed by the same two investigators independently using the eligibility criteria. Only those papers that fulfilled all the eligibility criteria were selected and entered into the third round.

In the third round (critical appraisal) each paper was critically appraised by the seven standards of Lau and Samman[9] to evaluate the quality of the methods used.

Data collection and data items

The following characteristics of all included studies were recorded: characteristics of the study (year and country), characteristics of the group studied (age range, sex distribution, radiographic findings, and mean size), surgical treatment, outcome, duration of follow up, and complications.

One investigator (MS) retrieved data from those studies included, and that was again independently checked by second investigator (SNG) and any difference between them were settled by their joint decision, and if not then finalised by the third investigator (KS).

Quality assessment: assessing risk of bias across the studies and within the studies Included

The quality of those studies finally included for analysis was assessed using the Lau and Samman[9] standards, which included seven standards for the critical appraisal of papers.

Those papers assessed were ranked into three categories (low, moderate, and high risk) according to the Cochrane reviewers' handbook, section 6.7.1.[10] Only papers with a low risk of bias were included in the final review. The search strategy was the same as described earlier for the two investigators.

Statistical analysis

Primer of Biostatistics software (version 7.0),[11] was used to estimate the recurrence rate and 95% CI for the significance of differences between overall and individual treatments. The chi squared test was calculated to assess the significance of any difference between conservative treatment and resection.

Results

Selection of studies

Ninety-eight papers were retrieved from the electronic sources, all from PubMed. Of the 98 abstract scanned, 77 were selected that related to both surgical treatment and recurrence of odontogenic myxoma. Cross-referencing of these 77 provided 19 more pertinent papers, resulting in a total of 96 available for evaluation. Of these 96, 82 did not fulfill one or more eligibility criteria and were therefore excluded, leaving 14 papers for critical appraisal.

Assessing risk of bias across and within studies

The quality of the study was assessed according to the criteria of Lau and Samman.[9] After analysis of the 14 papers according to the seven standards, 11 did not meet one or more standard because of risk bias; two of these had considerable bias,[3,13] and nine moderate bias,[5,12,14–21] and these were excluded (Table 1).

Three papers with low risk[22–24] were finally selected for critical appraisal and all three were retrospective (Table 2, Fig. 1). Data from these were taken for more detailed study.

Study characteristics

Year of study, author, geographical region, mean age, sex, cases included, radiographic findings, mean size, treatment, follow up period, recurrence, and complications associated with treatment and the treatment of recurrence were extracted (Table 3).

Summary of results

Of the 39 patients 12 were male and 27 female, M:F ratio 1:2.2, and ages ranged from 7 - 55 years (mean (SD) 28 (12) years).

Thirty tumours were reported to be in the mandible and nine in maxilla. Radiographic findings showed that the lesions were multilocular (n=30), and unilocular (n=7). In two cases the information was not given (Table 3).

Treatments were classified as conservative (curettage, enucleation with curettage, excision curettage, and excision) and resection.

Recurrence

The overall recurrence rate was 13% with a mean follow up period of 10 years. Details are shown in Table 4, and the difference was not significant. Details of the recurrences according to site are shown in Table 5.

Radiographic findings and recurrence

The 39 cases included seven unilocular lesions, and 30 multilocular lesions. In two cases radiographs were not available. Of the 30 multilocular lesions, 13 cases were described in one paper,[24] but there was no clear information available on the radiographic findings in respect to recurrence for these 13 cases, so they were not considered for further analysis of multilocular lesions and recurrence.

Among the unilocular lesions the incidence of recurrence was 20% after conservative treatment and 50% after

Table 1
Papers rejected after critical appraisal.

Year	First author and reference	Title	Reason for exclusion	Potential risk of bias
2017	Rowland[12]	Central myxoma/myxo fibroma of the jaws: a clinico-epidemiological review	Follow up less than five years	Moderate
2011	Effiom[14]	Clinicopathological Characteristics of odontogenic myxoma in Nigerians	Follow up period not mentioned	Moderate
2006	Dezotti[15]	Odontogenic myxoma – a case report and a clinico-radiographic study of seven tumors	Inadequate description of treatment in all cases	Moderate
2006	Li[16]	Odontogenic myxoma: a clinicopathological study of 25 cases	Follow up period less than five years	Moderate
2005	Adebayo[17]	A review of 318 odontogenic tumors in Kaduna, Nigeria	No adequate description of cases	Moderate
2004	Simon[3]	Odontogenic myxoma: a clinicopathological study of 33 cases	Follow up period not mentioned No comment about recurrences	High
1997	Arotiba[18]	Odontogenic tumours: a 15-year review from Ibadan, Nigeria	Description of treatment inadequate	Moderate
1996	Lo Muzio[5]	Odontogenic myxoma of jaws: a clinical, radiologic, immunohistochemical, and ultrastructural study	Follow up less than five years	Moderate
1987	Abiose[19]	Fibromyxomas of the jawbones–a study of 10 cases.	Follow up period less than five years	Moderate bias
1984	Adekeye[13]	Advanced central myxoma of the jaws in Nigeria: clinical features, treatment and pathogenesis	Follow up not mentioned. Recurrence not mentioned clearly	High
1978	Harder F[20]	Myxoma of the jaws	Inadequate description of treatment in all cases	Moderate

Table 2
Papers in which Lau and Sammon standards were fulfilled (n = 3).

Standards by Lau and Sammon	Francisco[22]	Boffano[23]	Slootweg[24]
1. Conduct of study adequate	Yes	Yes	Yes
2. Adequate description of selection of patients	Yes	Yes	Yes
3. Adequate diagnostic evaluation	Yes	Yes	Yes
4. Adequate description of follow-up, and explanation of reasons for withdrawal	Yes	Yes	Yes
5. Adequate description of treatment	Yes	Yes	Yes
6. Adequate documentation of adverse outcomes	Yes	Yes	Yes
7. Adequate clinical and demographic information	Yes	Yes	Yes
Bias	Low	Low	Low

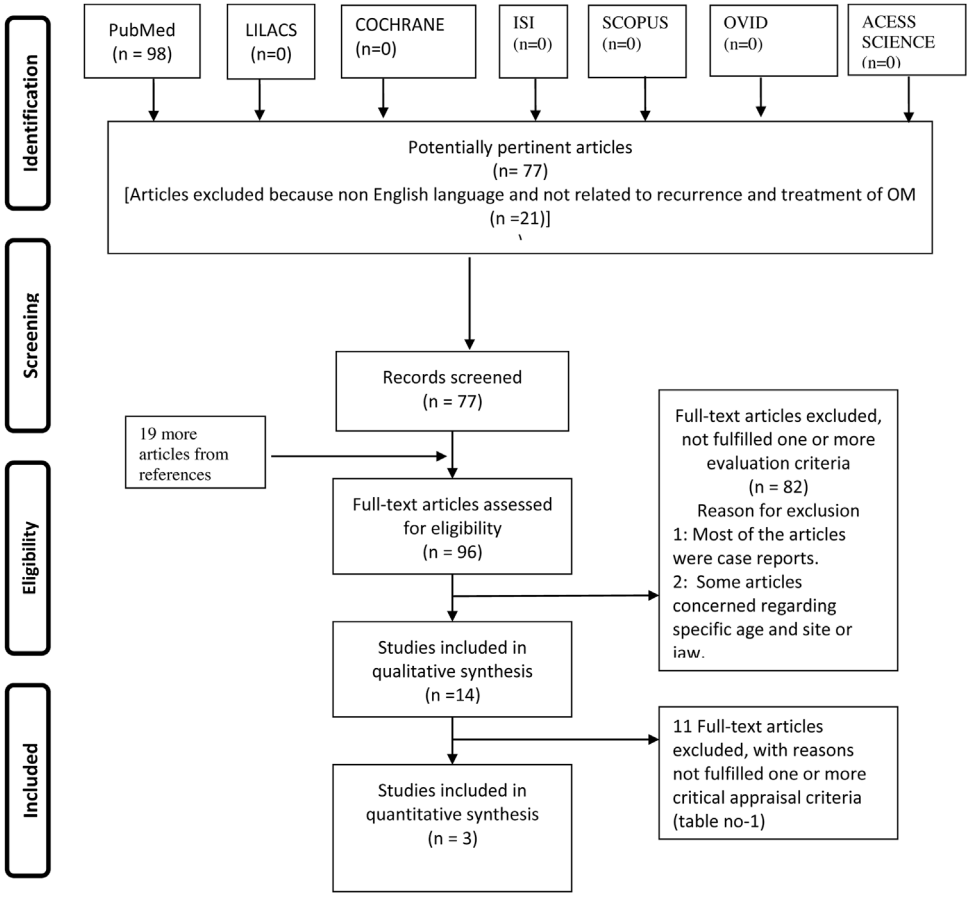

Fig. 1. PRISMA flow diagram showing search strategies.

resection. Multilocular lesions showed 25% recurrence after conservative treatment in contrast to none after resection.

Size and recurrence

Size and recurrence are shown in detail in Table 3.

Treatment of recurrences

Of the five recurrences (four after conservative treatment and one after resection), four were treated by extensive resection and showed no signs of further recurrence after a mean follow up of just over 11 years.

Discussion

Summary of evidence

The most prominent finding of this structured review was that overall, little has been published about the management of recurrences of odontogenic myxoma. We found no studies with good evidence such as meta-analyses, structured reports, or clinical trials. It has been reported that these tumours can recur after as long as 30 years,[20] so life-time follow-up is therefore advisable.[24] Most papers that we excluded did not clearly mention treatment and follow up, and if follow up was mentioned its mean or median duration was less than five years.

Table 3
Results of final analysis.

Variable	2017	2011	1986	Total
First author and reference	Francisco[22]	Boffano[23]	Slootweg[24]	–
Country of origin	Brazil	Italy	The Netherlands	–
No. of cases	14	10	15	39
Mean (SD) age (years):	22 (12)	40 (10)	26 (8)	28 (12)
Range	7-51	20-55	14-40	7-55
Sex (M/F)	3/11	6/4	3/12	12/27
Site:				
Maxilla	3	2	4	9
Mandible	11	8	11	30
Radiographic findings:				
Multilocular	9	8	13	30
Unilocular	5	2	–	7
Not known	–	–	2	2
Mean (SD) size (cm):	3.5 (1.3)	3.8 (1.02)	–	–
Range	2-6	2-5	–	–
Treatment:				
Curettage	10	–	–	10
Resection	4	7	6	17
Enucleation + curettage	–	3	6	9
Excision/curettage	–	–	2	2
Excision	–	–	1	1
Duration of follow-up in years(SD):	6.5 (6)	5.6 (4.5)	16 (10)	10 (9)
No. (%) recurrences:	4 (29)	0	1 (63)	5 (13)

Table 4
Different treatments with recurrence.

	Treatment	No. of patients	Recurrence and recurrence rate (95% CI)	Mean follow up period (years)	Chi squared test with Yates' correction
Conservative treatment recurrence rate 19% (95% CI 2.1% to 34.3%), mean follow up 10.9 years					
1	Excision	1	0	15	p = 0.51
2	Curettage	10	3 (30%) (1.6% to 58.4%)	6.3	
3	Enucleation and curettage	9	1 (11%) (0% to 31.6%)	12	
4	Excision curettage	2	0	27.5	
Resection treatment recurrence rate 6% (95% CI 0% to 17.1%), mean follow up 8.6 years					
5	Resection	17	1 (6%) (0% to 17.1%)	8.6	
Overall treatment recurrence rate (13%) (2.30% to 23.3%), mean follow up 10 years)					
Total	Overall	39	5 (13%) (2.3% to 23.3%)	10	

Table 5
Recurrences according to site and radiographic appearance.

	Site		Radiographic presentation		
	Maxilla n/N(%)	Mandible n/N(%)	Unilocular n/N(%)	Multilocular n/N(%)	2 NA, 13 NS n/N(%)
Conservative	0/3(0)	4/19(21.05)	1/5(20.0)	2/8(25.0)	1/9(11.11)
Resection	1/6(16.66)	0/11(0)	1/2(50.0)	0/9(0)	0/6(0)
	1/9(11.11)	4/30(13.33)	2/7(28.57)	2/17(11.76)	1/15(6.66)
Total cases (recurrence)	39(5)		39(5)		

n = Number of recurrent cases, N = total number of cases in particular category, NA = not available, NS = not specified.

Conservative treatment does not guarantee a recurrence-free follow up. Comparative analysis for each type of treatment could not be made because the number of patients varied in each category.

Various terms such as excision, excision curettage, and conservative excision, were used to describe different treatments, and there is a need for a consensus about the terminology used for treatments, and what would these indicate. We considered excision, excision curettage, and conservative excision as "conservative treatment".

Our interpretation of recurrence after conservative treatment concurs with that of Chrcanovic et al.[25] We found the incidence of recurrence after resection was 6%, which was higher than that found by Chrcanovic et al, which was 3.1% after segmental resection. This indicates a higher recurrence rate among global data.

More recurrences were associated with resection (1/6 cases) when compared with conservative (0/3 cases) treatment when the tumour was in the maxilla. This result should be taken with caution because of the under-representation of cases in the resection and conservative groups. In contrast, the incidence of mandibular recurrence was higher after conservative treatment (compared with no recurrence after resection), which suggests that resection could be the treatment of choice in the mandible.

Recurrence after resection in the maxilla was slightly higher than in the mandible, which could be attributed to the fact that in the maxilla the lesion has more scope to spread before it is clinically obvious. This finding should alert the clinician when treating maxillary myxomas.

Boffano et al[23] advised conservative treatment when the tumour was less than 3 cm. However, they had no recurrences in lesions of more than 3 cm that were treated conservatively, so size alone may not be the deciding factor for choice of the treatment.[26] We emphasise this because recurrence has been reported after even smaller lesions treated by curettage and resection, in comparison to slightly larger size lesions that were treated by enucleation with curettage and resection and which did not develop a recurrence.

Kauke et al[7] reported that multilocularity is significantly related to size, so it could be inferred that the chances of recurrence with larger lesions are greater if they are treated conservatively. However, because of lack of data on the recurrence rate they could not come to any conclusions about the relation between these factors and recurrence. We think that the margins of odontogenic myxomas could provide a vital clue to their recurrence because they are known to spread without causing immediate destruction. Given these findings, there is need to assess the size of the lesion, whether it is unilocular or multilocular, its margins (well-defined or ill-defined) and their relation to the recurrence rate. All these variables could best be assessed on radiographs, so preoperative radiographic assessment should therefore be done thoroughly to predict recurrence.

There was no significant difference in recurrence between conservative treatment and resection. It is also important to note that conservative treatment does not affect the patient's quality of life as much as resection. We therefore recommend that conservative treatment should be considered wherever possible to provide optimal quality of life for the patient.

It could be argued that resection results in a lower recurrence rate, but it has disadvantages such as compromised function, and aesthetic morbidity. Temporary and permanent deficit of the inferior alveolar nerve have been associated with resection when compared with conservative treatment. It could also be associated with loss of function (including mastication and speech), and facial disfigurement that affects the patient's quality of life. However these quality of life variables have not been evaluated yet and should be considered in future studies.

Limitations

We found that the radiographic findings were not clearly mentioned in some cases, so it was not possible to correlate recurrence with its associated radiographic findings. A clear definition of the treatment used and the size of the tumour could have also improved the results.

Conclusion

The recurrence rate was relatively low over 10 years of follow up, irrespective of whether resection or a more conservative approach was used, and was slightly lower, as might be expected, with resection. Conservative treatment could be considered first to avoid both morbidity and resection-associated effects on the quality of life. Maxillary lesions have more room to spread before they are clinically evident, which makes it difficult to treat them optimally, and contributes to the recurrence rate.

Conflict of interest

We have no conflicts of interest.

Ethics statement/confirmation of patients' permission

Ethics approval not needed. Patients' informed consent not needed in structured reviews.

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