Int. J. Oral Maxillofac. Surg. 2019; 48: 1300–1306
https://doi.org/10.1016/j.ijom.2019.04.008, available online at https://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Clinical Paper
Clinical Pathology

Risk factors for recurrence of ameloblastoma: a long-term follow-up retrospective study

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S. W. Au, K. Y. Li, W. S. Choi, Y. X. Su: Risk factors for recurrence of ameloblastoma: a long-term follow-up retrospective study. Int. J. Oral Maxillofac. Surg. 2019; 48: 1300–1306.

Abstract. Ameloblastoma is a benign odontogenic tumour showing locally aggressive characteristics. This retrospective study was performed to investigate the long-term treatment outcomes of ameloblastoma and to evaluate the risk factors for recurrence. The study was conducted in the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, the University of Hong Kong and covered the years 1990–2017. Patient demographic data, radiographic pattern and findings, clinical findings, tumour site and size, World Health Organization classification, treatment modality, histological pattern, duration of follow-up, and timing of recurrence were recorded and analyzed. The potential risk factors were analyzed by Kaplan–Meier and Cox regression tests. The cases of a total of 128 patients were reviewed; 65 were male and 63 were female. The mean follow-up period was 117 months. The 5-, 10-, and 15-year recurrence rates were 9.3%, 17.6%, and 24.4%, respectively. Kaplan–Meier and Cox regression tests showed that recurrence was significantly associated with radiographic pattern, tumour size, and treatment modality. Multiple regression analysis for these three variables demonstrated that treatment modality was the only independent prognostic factor for recurrence. This study showed that radical resection is the only significant factor for a low recurrence rate of ameloblastoma and patients require long-term follow-up for late-onset recurrence.

Key words: ameloblastoma; recurrence; risk factor; head and neck.

Accepted for publication
Available online 11 May 2019

Ameloblastoma is a benign odontogenic tumour. It is defined by the World Health Organization (WHO) as a tumour formed by odontogenic epithelium with mature, fibrous stroma without odontogenic ectomesenchyme[1]. In 2017, the WHO classification of ameloblastoma was updated to include four subtypes[2]. These are (1) peripheral/extraosseous ameloblastoma, (2) unicystic ameloblastoma, (3) ameloblastoma (conventional), and (4) metastasizing ameloblastoma.

Conventional ameloblastoma (which was called 'solid/multicystic type') is the most common variant and it invades the bone marrow spaces. It often occurs in the posterior mandible and usually appears multilocular in radiographs. The two most commonly seen histological patterns are plexiform and follicular. The others are acanthomatous, desmoplastic, granular, and basal[3]. Unicystic ameloblastoma forms a cystic cavity defined by ameloblastomatous epithelium[4,5]. It usually appears unilocular in radiographs[6]. In 1988, Ackerman et al. regrouped unicystic ameloblastoma into three subtypes, namely luminal, intraluminal, and mural type. They reported that the cystic lining of unicystic ameloblastoma may show fea-

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tures of conventional ameloblastoma in focal regions[7].

Although ameloblastoma has a benign nature, it is aggressive due to its local invasiveness and high recurrence rate. With conservative treatment, a recurrence rate of up to 55–90% has been reported[5,8,9]. Recurrent and long-duration tumours might transform into ameloblastic carcinomas[10]. Although resection can lower the tumour recurrence rate[11–13], it jeopardizes functional and cosmetic outcomes of the jaws. There may also be the need for a donor site for reconstruction. Therefore, there are arguments over the best treatment modality[14].

Identifying the risk factors for recurrence can help with clinical decision-making, prediction of the prognosis, and follow-up. Therefore, the aim of this study was to investigate the long-term recurrence rate of ameloblastoma and to evaluate the risk factors for recurrence, including clinical, radiographic, and histopathological features, at a single institution over a 27-year period.

Materials and methods

Study design

This study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster. All patients with pathologically confirmed ameloblastoma treated in the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, the University of Hong Kong from 1990 to 2017 were recruited, without age restriction. Patients who were followed up for less than 1 year after surgery were excluded.

The data collection included: (1) age, divided into three groups: $\leq$30 years old, 31–50 years old, and $\geq$51 years old. (2) Tumour site, for which four different locations were considered: anterior maxilla (canine to canine), posterior maxilla (premolar to tuberosity), anterior mandible (canine to canine), and posterior mandible (premolar to ramus up to condyle). (3) Radiographic findings, with radiographic patterns divided into three groups: unilocular radiolucency, multilocular radiolucency, and others (no radiolucency or mixed radiolucent–radiopaque lesions). The presence of root resorption, impacted tooth involvement, and pathological fracture was also recorded. (4) Histological patterns and features, grouped into plexiform, follicular, unicystic (luminal, intraluminal, and mural), and others (granular cell, basal cell, desmoplastic, and acanthomatous). The most prominent histological pattern observed was recorded as the dominant pattern. The presence of cortical bone involvement was examined radiographically and histopathologically. The presence of soft tissue infiltration was recorded from the histopathology reports. (5) Tumour size, which was recorded by measuring the greatest dimension of the final specimen. (6) The final diagnosis, determined from the histopathology report. This was grouped according to the WHO classification. (7) Treatment modality, grouped into marsupialization, enucleation only, enucleation with Carnoy's solution, and radical treatment (resection). Marsupialization was mainly employed when the lesion was large in size, as this might jeopardize the adjacent vital structures or cause pathological fracture during enucleation. Enucleation only was employed during the excisional biopsy for small-size unilocular lesions. Enucleation with Carnoy's solution was performed for biopsy-confirmed unicystic ameloblastoma, or conventional ameloblastoma in patients who opted for conservative treatment. Resection was used to treat conventional ameloblastoma. (8) Follow-up, which was dated from the time of first treatment to the latest follow-up date. (9) Recurrence, dated from the time of first treatment to the date when recurrence was confirmed histopathologically. Only the first recurrence was investigated in this study.

Statistical analysis

The statistical analysis was performed using IBM SPSS Statistics version 24.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics including the mean, standard deviation, and median values were determined for continuous variables. The Kaplan–Meier estimate was used to calculate the recurrence rates. Univariate analysis, the log rank test (for categorical variables), or Cox regression (for continuous variables) was first used to evaluate the relationships between the risk factors and recurrence one by one. The corresponding hazard ratios (HR) with 95% confidence intervals (CI) were also estimated by separated univariate Cox regressions. Kaplan–Meier curves were generated for the significant risk factors. Final multivariate Cox regression was then performed to include all significant factors in the univariate analyses. Results were considered statistically significant when the P-value was <0.05.

Results

One hundred and thirty-nine patients were diagnosed with ameloblastoma in the study department during the years 1990–2017. Eleven patients were excluded from the study due to loss to follow-up within 1 year. Twenty-two patients were confirmed with recurrent ameloblastoma.

Patient demographics and clinical characteristics

A total of 128 patients were recruited in total. The mean follow-up period was 117 months (median 102 months, range 14–345 months). The mean lesion size was 36.4 mm (median 31 mm, range 10–130 mm). There were 65 male patients and 63 female patients (ratio of 1:1.03). The total number of tumours was 128. Eighty-seven tumours were located in the posterior mandible (68.0%), 29 in the anterior mandible (22.7%), seven in the anterior maxilla (5.5%), and five in the posterior maxilla (3.9%). Nearly half of the patients (49.2%) were in the age group of $\leq$30 years, while 33.6% of patients were 31–50 years old and 17.2% were over 50 years old. The demographic data of these 128 patients are presented in Table 1.

WHO classification

Seventy-eight cases (60.9%) were confirmed to be conventional ameloblastoma and 49 cases (38.3%) were unicystic ameloblastoma. Only one case (0.8%) of peripheral ameloblastoma was diagnosed. No metastasizing ameloblastoma was recorded.

Initial treatment modalities

Seventy-seven cases (60.2%) were treated by radical resection including segmental or marginal resection of the jaw, 43 cases (33.6%) were treated by enucleation with Carnoy's solution application, and seven cases (5.5%) were treated with enucleation only. Only one case (0.8%) was treated by marsupialization.

Radiological–pathological characteristics (Table 2)

Only 120 of the recruited patients had panoramic radiographs. Three cases (2.5%) showed no radiographic radiolucency, 57 cases (47.5%) showed unilocular radiolucency, 54 cases (45.0%) showed multilocular radiolucency, and six cases (5.0%) showed features of mixed radiolucent and radiopaque lesions.

Histologically, 28 cases (29.8%) were identified as follicular pattern and 26 cases (27.7%) as plexiform pattern. Other sub-

Table 1. Patient demographics and clinical characteristics, WHO classification, and treatment modalities.

Variables and categories	Total number	Number with recurrence	% with recurrence	HR	95% CI	*P*-value
Age (years)						0.362
≤30	63	12	19.0	Ref.		
31–50	43	8	18.6	0.79	0.32–1.94	0.599
≥51	22	2	9.1	0.35	0.08–1.58	0.173
Sex						
Male	65	11	16.9	Ref.		
Female	63	11	17.5	0.96	0.41–2.23	0.923
Site						0.739
Anterior maxilla	7	1	14.3	Ref.		
Posterior maxilla	5	0	0.0	0	0	0.985
Anterior mandible	29	5	17.2	1.37	0.16–11.73	0.772
Posterior mandible	87	16	18.4	1.54	0.20–11.68	0.673
Tumour size, for every 10-mm increase (continuous)				1.26	1.00–1.57	0.049
Treatment						<0.001
Marsupialization[a]	1	1	100.0			
Enucleation only	7	7	100.0	24.46	7.44–80.35	<0.001
Enucleation with Carnoy's solution application	43	9	20.9	4.49	1.50–13.45	0.004
Radical treatment	77	5	6.5	Ref.		
WHO classification						0.918
Unicystic ameloblastoma	49	7	14.3	Ref.		
Peripheral ameloblastoma	1	0	0.0	0	0	0.983
Conventional ameloblastoma	78	15	19.2	1.13	0.46–2.78	0.789
Metastasizing ameloblastoma	0					

WHO, World Health Organization; HR, hazard ratio; CI, confidence interval; Ref., reference category.
[a] Marsupialization was not included in the Cox regression test, as only one case was present.

Table 2. Radiological and pathological characteristics and other features.

Variables and categories	Total number	Number with recurrence	% with recurrence	HR	95% CI	*P*-value
Radiographic pattern						0.020
Unilocular	57	12	21.1	Ref.		
Multilocular	54	3	5.6	0.22	0.06–0.79	0.020
Other (mixed radiolucent–radiopaque and no radiolucency)	9	0	0.0	0	0	0.986
Histological type						0.954
Plexiform	26	4	15.4	Ref.		
Follicular	28	4	14.3	0.79	0.20–3.17	0.738
Other (granular, basal cell, desmoplastic, and acanthomatous)[a]	9	2	22.2	1.18	0.21–6.61	0.846
Unicystic[b]	31	4	12.9	0.80	0.20–3.20	0.747
Cortical bone invasion						
No	33	2	6.1	Ref.		
Yes	89	15	16.9	0.45	0.10–1.98	0.277
Root resorption						
No	72	11	15.3	Ref.		
Yes	50	6	12.0	0.66	0.24–1.78	0.404
Impacted tooth						
No	84	10	11.9	Ref.		
Yes	38	7	18.4	1.61	0.61–4.24	0.328
Soft tissue infiltration						
No	84	11	13.1	Ref.		
Yes	36	6	16.7	0.94	0.34–2.59	0.906
Pathological fracture						
No	119	17	14.3	Ref.		
Yes	2	0	0.0	0.05	0	0.679

HR, hazard ratio; CI, confidence interval; Ref., reference category.
[a] Granular, basal cell, desmoplastic, and acanthomatous subgroups were grouped into one subgroup for the data analysis.
[b] Intraluminal, luminal, and mural were grouped into the unicystic subgroup for the data analysis.

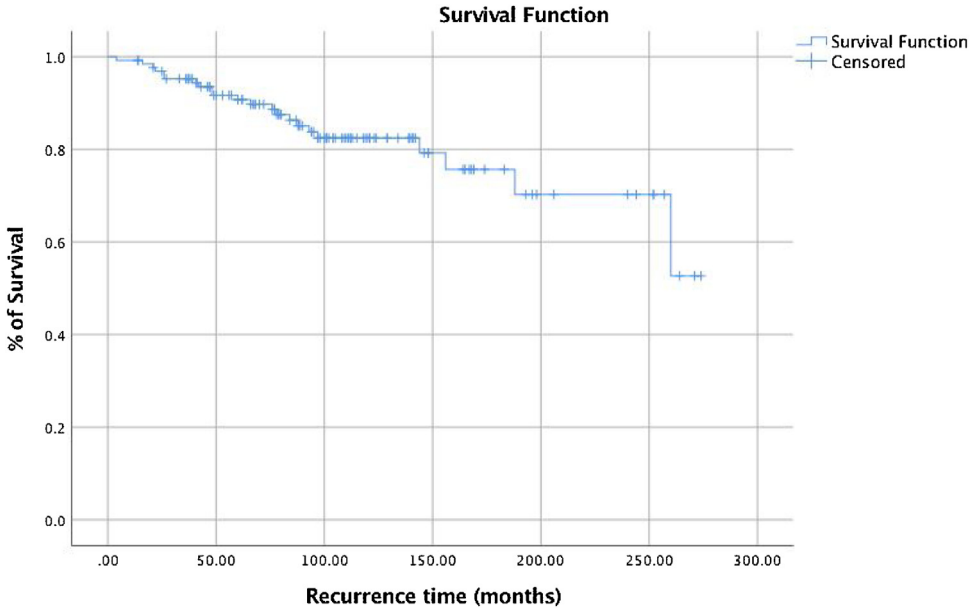

Fig. 1. Kaplan–Meier survival function curve for recurrence time.

types (granular cell, basal cell, desmoplastic, and acanthomatous) could only be identified in nine cases (9.6%). Thirty-one cases (33.0%) were of unicystic subtype. Specifically, the mural subtype accounted for 80.6% of the unicystic ameloblastomas.

Cortical bone invasion was the most common finding and was identified in 89 out of 122 cases (73.0%), followed by root resorption (50 cases, 41.0%). Thirty-eight cases (31.1%) had impacted tooth involvement within the tumour. Most of the impacted teeth involved were third molars. Soft tissue infiltration was detected in 36 cases (30.0%). Only two cases (1.7%) had reported pathological fracture.

Forty-eight cases of unicystic ameloblastoma had radiographs for interpretation, with 68.8% displaying unilocular radiolucency and 31.3% displaying multilocular radiolucency. Radiographs were available for 71 cases of conventional ameloblastoma, with 33.8% displaying unilocular radiolucency and 66.2% displaying multilocular radiolucency.

Recurrence and risk factors

Recurrence occurred in 22 cases (17.2%). The 5-, 10-, and 15-year recurrence rates according to Kaplan–Meier analysis were 9.3%, 17.6%, and 24.4%, respectively (Fig. 1).

Tumour size was significantly associated with recurrence ($P = 0.049$) (Table 1). The mean tumour size was 36.4 mm and the Kaplan–Meier curve for the mean tumour size is presented in Fig. 2. For every 10-mm increase in tumour size, there was a 1.26-fold increased hazard ratio of recurrence. The radiographic pattern and treatment modality were also statistically significant factors associated with recurrence ($P = 0.02$ and $P < 0.001$, respectively) (Tables 1 and 2, Figs 3 and 4). Tumours with multilocular radiolucency had a 78% reduced hazard ratio of recurrence when compared to those with unilocular radiolucency (HR 0.22, 95% CI 0.06–0.79, $P = 0.020$). Cases treated by enucleation only were associated with

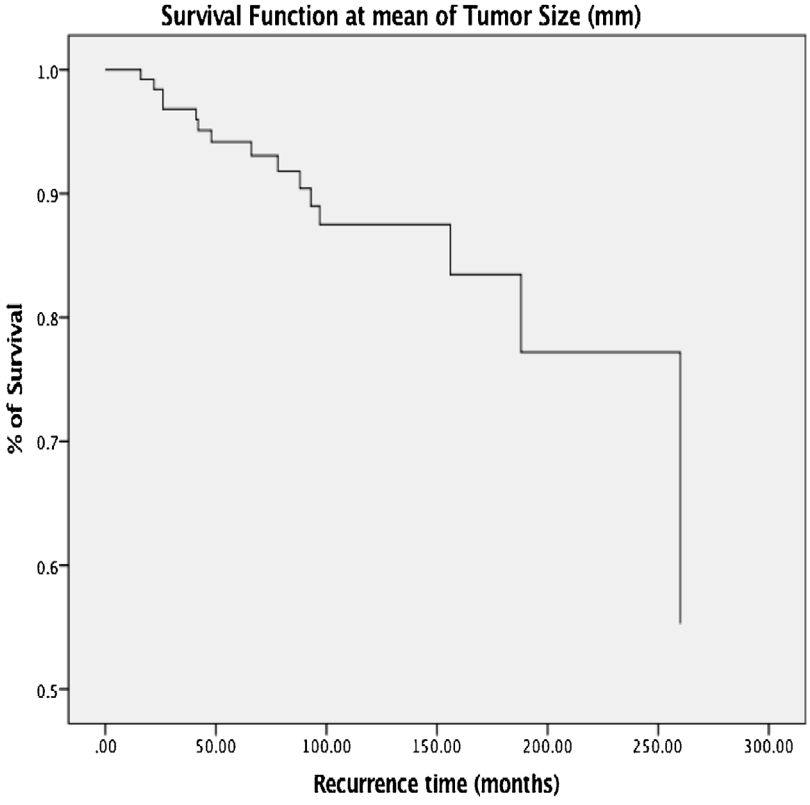

Fig. 2. Disease-free survival function curve for tumour size.

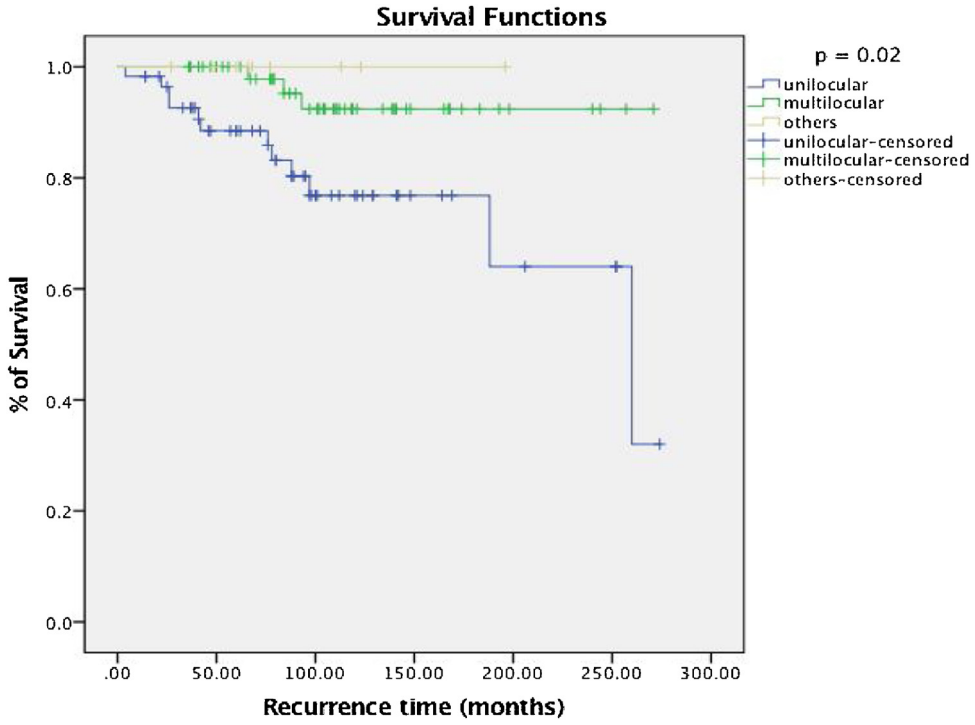

Fig. 3. Disease-free survival function curves for radiographic pattern. The results show that unilocular radiolucent lesions had a higher recurrence rate than multilocular radiolucent lesions.

24.46 times the hazard of recurring compared to those treated by radical treatment ($P < 0.001$). Cases treated by enucleation with Carnoy's solution were associated with 4.49 times the hazard of recurring compared to those treated by radical treatment ($P = 0.004$). No other variable showed a statistically significant relationship with recurrence.

With regard to the mural type, there was a significantly lower risk of recurrence when treated by resection than when treated with enucleation with Carnoy's solution ($P = 0.046$). For the follicular subtype, both resection and enucleation with Carnoy's solution led to a significantly lower recurrence risk than treatment by enucleation only ($P < 0.001$ and $P = 0.019$, respectively).

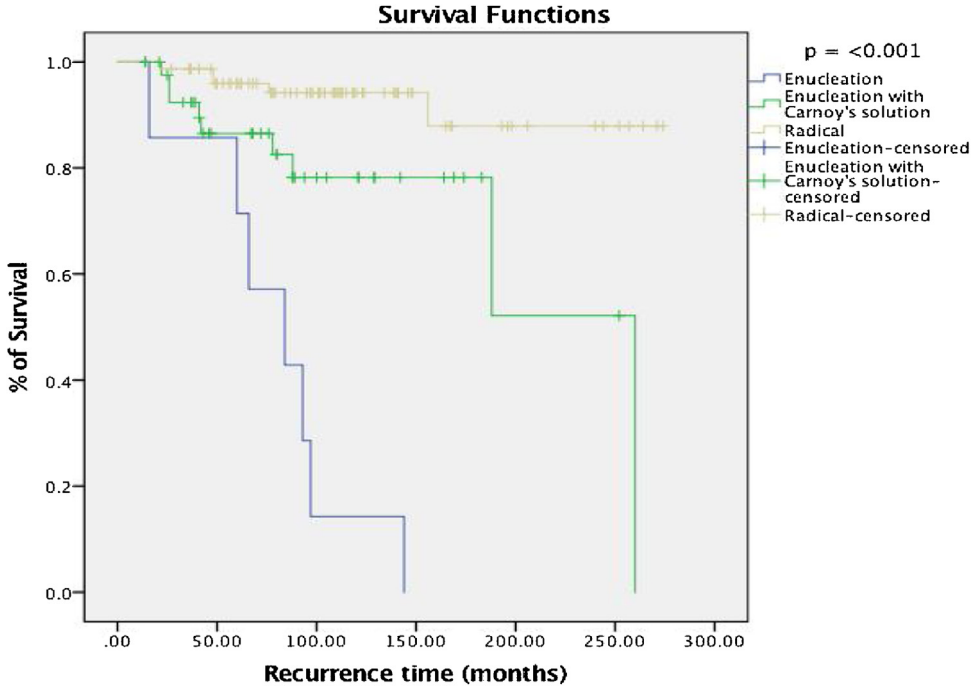

Fig. 4. Disease-free survival function curves for treatment methods. The results show that radical treatment had the lowest recurrence rate.

Multiple regression analysis was performed for the three significant variables, i.e., radiographic pattern, tumour size, and treatment modality. It was found that treatment modality remained significant ($P < 0.05$), while radiographic pattern ($P = 0.69$) and tumour size were non-significant ($P = 0.38$). Therefore, treatment modality was shown to be an independent prognostic factor for the recurrence of ameloblastoma.

Discussion

The study results revealed that the 5-, 10-, and 15-year recurrence rates for ameloblastoma were 9.3%, 17.6%, and 24.4%, respectively. Statistically significant factors associated with recurrence were treatment modality, radiographic pattern, and tumour size, among which only treatment modality was found to be an independent prognostic factor.

The incidence of ameloblastoma recurrence in this study is comparable to those reported in previous studies, which are within the range of 15.9% to 20.6%[15,16]. The tumour occurred most frequently in the posterior mandible, which is in line with the results of others[15,16,17–19]. The prevalence according to sex showed a male to female ratio of 1:1.03. Most previous studies have shown similar ratios[15,16,20]. The proportion of unicystic ameloblastoma was 38.3%, which is higher than that reported in previous studies[15,21]. It has generally been believed that unicystic ameloblastoma demonstrates unilocular radiolucency[6]. The present study showed that unicystic ameloblastoma also presented as multilocular lesions. Interestingly, conventional ameloblastoma might also present as unilocular radiolucency. Therefore, histological examination remains the gold standard for diagnosis.

This study confirmed that the recurrence rate of ameloblastoma was lower with more aggressive treatment. The rate was lowest for lesions treated with radical resection, followed by those treated with enucleation with Carnoy's solution application. Lesions treated with enucleation showed the highest recurrence rate. This is in accordance with the findings of the majority of other studies[22,23]. Carnoy's solution lowers the recurrence rate by fixation of the surrounding tissues of the cavity and penetrating into microscopically infiltrated regions. Lau and Samman reported a recurrence rate of 16% with the use of Carnoy's solution as adjunctive treatment when compared to a recurrence rate of 30.5% with the use of enucleation alone in the treatment of unicystic ameloblastoma[24]. The use of Carnoy's solution is controversial. The US Food and Drug Administration has banned the use of Carnoy's solution since 1992 due to the presence of chloroform, i.e., a carcinogenic agent. Yet, the use of Carnoy's solution is still allowed and accepted in Hong Kong. This study confirmed that Carnoy's solution significantly reduced the recurrence rate. Dashow et al. reported significantly decreased recurrence rates in keratocystic odontogenic tumour with enucleation using Carnoy's versus modified Carnoy's solution[25]. However, there is currently no evidence of the effectiveness of modified Carnoy's solution in the treatment of ameloblastoma.

Interestingly, it was found that ameloblastoma with a unilocular radiographic pattern had a higher recurrence rate than multilocular lesions. A possible explanation for this is that some small unilocular tumours possessed the features of conventional ameloblastoma histologically, yet these lesions were treated conservatively, leading to a higher recurrence rate. Unicystic ameloblastoma with a mural subtype could penetrate into bone through the cystic cavity. It has been proposed that this subtype is treated as for conventional ameloblastoma[7]. The results of the present study also showed that ameloblastoma with the mural subtype treated by radical resection had a significantly lower recurrence rate. The mural subtype could only be identified by meticulous serial histological examination of the specimen. However, incisional biopsy does not represent the whole lesion. Consequently, the diagnosis of mural subtype ameloblastoma might be missed during incisional biopsy. The present study results revealed that a high percentage of unicystic ameloblastoma (80.6%) was of the mural type in the final histopathology report. Ackermann et al. reported that 49% of unicystic ameloblastoma belonged to the mural subtype[7], while Lee and Samman reported a very high percentage (93%) of unicystic lesions exhibiting mural invasion also in a Hong Kong population[26]. Whether this disparity is due to the difference in ethnicity or variations in diagnostic criteria in different pathology laboratories remains unclear. Those with a unilocular radiographic pattern who were misdiagnosed with a non-mural type on incisional biopsy were treated conservatively, thereby leading to a higher recurrence rate.

This study found that there was a significant relationship between tumour size and the recurrence rate of ameloblastoma. There was 1.26-fold increased risk of recurrence for every 10-mm increase in size of the tumour. A study by Yang et al. found that tumours larger than 60 mm were associated with a higher recurrence rate[27]. Fregnani et al., however, reported no significant relationship between tumour size and recurrence[23]. Further studies with a higher level of evidence are necessary to verify this risk factor.

There is controversy concerning whether lesions with a follicular histological pattern have a higher recurrence rate[12,23,28]. The present study could find no association between the histological pattern and recurrence. Reichart et al. reported that 15.5% of ameloblastomas consisted of mixed histological patterns[15]. All currently available studies used the predominant histological pattern as the representative pattern. This might have led to an underestimate of the effect exerted by a neglected, non-predominant histological pattern. Studying the non-predominant histological patterns of the samples might be required to gain a better understanding of this relationship.

Marsupialization has not been conducted routinely in the study department over the past 20 years. Thus, in this study, it was excluded from the analysis. A recent retrospective study showed promising results for marsupialization in 44 cases of mandibular cystic ameloblastoma (75% of which were unicystic), with a recurrence rate of 4.5%[29]. However, this recurrence rate might be greatly underestimated, since the average follow-up period in that study was only 4 years and the recurrence rate is expected to increase over the follow-up period, as revealed in the present study. Therefore, more long-term follow-up studies are needed to reach a convincing conclusion.

In general, this study is in agreement with previous studies and supports radical treatment as the treatment of choice for ameloblastoma[22,27,30]. However, there are many other factors to consider when deciding on the treatment modality, including the patient's age, general condition, financial issues, follow-up compliance, adjacent vital structures, aesthetics, patient preference, surgeon expertise, the availability of medical facilities, social issues, recurrence, and whether the tumour is a primary tumour, among others. All of these should be considered in order to provide the best treatment for each individual patient.

In conclusion, this article reports the results of a retrospective study with long-term follow-up on the treatment outcomes of ameloblastoma and the risk factors for recurrence. The 5-, 10-, and 15-year recurrence rates were 9.3%, 17.6%, and 24.4%, respectively. The initial treatment

modality, tumour size, and radiographic pattern showed significant associations with the risk of recurrence, while radical resection was the only independent predictive factor for a reduced risk of recurrence. Most ameloblastomas recurred within 5–6 years, yet late recurrence up to 20 years was evident. Therefore, the long-term follow-up of all patients with ameloblastoma is warranted.

Declarations

The following additional information is required for submission. Please note that failure to respond to these questions/statements will mean your submission will be returned to you. If you have nothing to declare in any of these categories then this should be stated.

Funding

This study has no funding source.

Competing interests

The authors have no conflict of interest to declare.

Ethical approval

Ethical approval was given by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (Number UW17-321).

Patient consent

Not required.

References

1. Barnes L, Eveson JW, Reichart P, Sidransky D. *World Health Organization classification of tumours. Pathology and genetics of the head and neck tumours*. Lyon: IARC Press; 2005: 283–327.
2. Wright JM, Vered M. Update from the 4th edition of the World Health Organization classification of head and neck tumours: odontogenic and maxillofacial bone tumors. *Head Neck Pathol* 2017;**11**:68–77.
3. Wright JM, Tekkesin MS. Odontogenic tumors: where are we in 2017? *J Istanb Univ Fac Dent* 2017;**51**(Suppl. 1 (3)):S10–30.
4. Philipsen HP, Reichart PA. Unicystic ameloblastoma. A review of 193 cases from the literature. *Oral Oncol* 1998;**34**:317–25.
5. Robinson L, Martinez MG. Unicystic ameloblastoma: a prognostically distinct entity. *Cancer* 1977;**40**:2278–85.
6. Abrams AM, Melrose RJ, Handlers JP. Oral pathology: unicystic ameloblastoma. *J Calif Dent Assoc* 1990;**18**:76–7.
7. Ackermann GL, Altini M, Shear M. The unicystic ameloblastoma: a clinicopathological study of 57 cases. *J Oral Pathol* 1988;**17**:541–6.
8. Gardner DG, Corio RL. Plexiform unicystic ameloblastoma. A variant of ameloblastoma with a low-recurrence rate after enucleation. *Cancer* 1984;**53**:1730–5.
9. Emmings FG, Gage AA, Koepf SW. Combined curettage and cryotherapy for recurrent ameloblastoma of the mandible: report of case. *J Oral Surg* 1971;**29**:41–4.
10. Clay RP, Weiland LH, Jackson IT. Ameloblastoma metastatic to the lung. *Ann Plast Surg* 1989;**22**:160–2.
11. Becelli R, Carboni A, Cerulli G, Perugini M, Iannetti G. Mandibular ameloblastoma: analysis of surgical treatment carried out in 60 patients between 1977 and 1998. *J Craniofac Surg* 2002;**13**:395–400.
12. Hong J, Yun PY, Chung IH, Myoung H, Suh JD, Seo BM, Lee JH, Choung PH. Long-term follow up on recurrence of 305 ameloblastoma cases. *Int J Oral Maxillofac Surg* 2007;**36**:283–8.
13. Sham E, Leong J, Maher R, Schenberg M, Leung M, Mansour AK. Mandibular ameloblastoma: clinical experience and literature review. *ANZ J Surg* 2009;**79**:739–44.
14. Almeida Rde AC, Andrade ES, Barbalho JC, Vajgel A, Vasconcelos BC. Recurrence rate following treatment for primary multicystic ameloblastoma: systematic review and meta-analysis. *Int J Oral Maxillofac Surg* 2016;**45**:359–67.
15. Reichart PA, Philipsen HP, Sonner S. Ameloblastoma: biological profile of 3677 cases. *Oral Oncol* 1995;**31B**:86–99.
16. Ledesma-Montes C, Mosqueda-Taylor A, Carlos-Bregni R, de León ER, Palma-Guzmán JM, Páez-Valencia C, Meneses-Garcia A. Ameloblastomas: a regional Latin-American multicentric study. *Oral Dis* 2007;**13**:303–7.
17. Jing W, Xuan M, Lin Y, Wu L, Liu L, Zheng X, Tang W, Qiao J, Tian W. Odontogenic tumours: a retrospective study of 1642 cases in a Chinese population. *Int J Oral Maxillofac Surg* 2007;**36**:20–5.
18. Avelar RL, Antunes AA, Santos Tde S, Andrade ES, Dourado E. Odontogenic tumors: clinical and pathology study of 238 cases. *Braz J Otorhinolaryngol* 2008;**74**:668–73.
19. Luo HY, Li TJ. Odontogenic tumors: a study of 1309 cases in a Chinese population. *Oral Oncol* 2009;**45**:706–11.
20. Lu Y, Xuan M, Takata T, Wang C, He Z, Zhou Z. Odontogenic tumors. A demographic study of 759 cases in a Chinese population. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998;**86**:707–14.
21. Olaitan AA, Adekeye EO. Unicystic ameloblastoma of the mandible: a long term follow up. *J Oral Maxillofac Surg* 1997;**55**:345–348.
22. Carlson ER, Marx RE. The ameloblastoma: primary, curative surgical management. *J Oral Maxillofac Surg* 2006;**64**:484–94.
23. Fregnani ER, da Cruz Perez DE, de Almeida OP, Kowalski LP, Soares FA, de Abreu Alves F. Clinicopathological study and treatment outcomes of 121 cases of ameloblastomas. *Int J Oral Maxillofac Surg* 2010;**39**:145–9.
24. Lau SL, Samman N. Recurrence related to treatment modalities of unicystic ameloblastoma: a systematic review. *Int J Oral Maxillofac Surg* 2006;**35**:681–90.
25. Dashow JE, McHugh JB, Braun TM, Edwards JP, Helman JI, Ward BB. Significantly decreased recurrence rates in keratocystic odontogenic tumor with simple enucleation and curettage using Carnoy's versus modified Carnoy's solution. *J Oral Maxillofac Surg* 2015;**73**:2132–5.
26. Lee PK, Samman N, Ng IO. Unicystic ameloblastoma—use of Carnoy's solution after enucleation. *Int J Oral Maxillofac Surg* 2004;**33**:263–7.
27. Yang R, Liu Z, Gokavarapu S, Peng C, Ji T, Cao W. Recurrence and cancerization of ameloblastoma: multivariate analysis of 87 recurrent craniofacial ameloblastoma to assess risk factors associated with early recurrence and secondary ameloblastic carcinoma. *Chin J Cancer Res* 2017;**29**:189–195.
28. Milman T, Ying GS, Pan W, LiVolsi V. Ameloblastoma: 25 year experience at a single institution. *Head Neck Pathol* 2016;**10**:513–20.
29. Yang Z, Liang Q, Yang L, Zheng GS, Zhang SE, Lao XM, Liang YJ, Liao GQ. Marsupialization of mandibular cystic ameloblastoma: retrospective study of 7 years. *Head Neck* 2018;**40**:2172–80.
30. Nakamura N, Higuchi Y, Mitsuyasu T, Sandra F, Ohishi M. Comparison of long-term results between different approaches to ameloblastoma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002;**93**:13–20.

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