Ameloblastic fibroma and ameloblastic fibrosarcoma: a systematic review

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ABSTRACT

Purpose. To integrate the available data published to date on ameloblastic fibromas (AF) and ameloblastic fibrosarcomas (AFS) into a comprehensive analysis of their clinical/radiologic features.

Methods. An electronic search was undertaken in July/2017. Eligibility criteria included publications having enough clinical, radiological and histological information to confirm a definite diagnosis.

Results. 244 publications (279 central AF tumours, 10 peripheral AF, 103 AFS) were included.

AF and AFS differed significantly with regard to the occurrence of patients' mean age, bone expansion, cortical bone perforation and lesion size. Recurrence rates were: central AF (19.2%), peripheral AF (12.5%), AFS (all lesions, 35%), primary (*de novo*) AFS (28.8%), secondary AFS (occurring after an AF, 50%). Larger lesions and older patients were more often treated by surgical resections for central AF. Segmental resection resulted in the lowest rate of recurrence for most of the lesion types. AFS treated by segmental resection had a 70.5% lower probability to recur (OR 0.295; $p=0.049$) than marginal resection. 21.3% of the AFS-patients died due to complications related to the lesion.

Conclusions. Very long follow-up is recommended for AF lesions, due to the risk of recurrence and malignant change into AFS. Segmental resection is the most recommended therapy for AFS.

KEYWORDS

Ameloblastic fibroma; ameloblastic fibrosarcoma; odontogenic tumors; clinical features; recurrence rate

INTRODUCTION

The ameloblastic fibroma (AF) is a tumour composed of odontogenic ectomesenchyme resembling the dental papilla with epithelial strands and nests similar to the dental lamina and enamel organ, but with no dental hard tissues. The ameloblastic fibrosarcoma (AFS) is a neoplasm with a similar structure to the AF, but composed of a benign epithelium and a malignant

mesenchymal component - typically comprising marked cellularity, nuclear pleomorphism and a moderate to high number of mitotic figures - i.e. the mesodermal component shows features of sarcoma (1). AFS is considered to be the malignant counterpart of AF.

AF represents only about 2% of odontogenic tumours (2), and AFS is considered to be rare. An epidemiological study of these rare tumours is important because it provides information that can improve diagnostic accuracy, allowing pathologists and surgeons to make informed decisions and refine treatment plans to optimize clinical outcomes (3-5). Therefore, the aim of the present study was to integrate the available data published in the literature on these lesions into an updated comprehensive comparative analysis of their clinical and radiologic features, as well as the frequency of recurrence.

MATERIALS AND METHODS

This study followed the PRISMA Statement guidelines (6).

Search strategies

An electronic search without time restrictions was undertaken and last updated in July 2017 in the following databases: PubMed/Medline, Web of Science, Science Direct, J-Stage, and LILACS. The following terms were used in the search strategies:

(ameloblastic fibroma) OR (ameloblastic fibrosarcoma) OR (ameloblastic sarcoma)

Google Scholar was also checked. A manual search of all related oral pathology, maxillofacial and specialist and oral journals was performed. The reference list of identified studies and the relevant reviews on the subject were also checked for possible additional studies. Publications with lesions identified by other authors as being AF or AFS, even not having the term “ameloblastic

fibroma“ or “ameloblastic fibrosarcoma” in the title of the article, were also re-evaluated by an author (RSG) of the present study.

Inclusion and Exclusion Criteria

Eligibility criteria included publications reporting cases of AF or AFS. The studies needed to contain enough clinical, radiological and histological information to confirm the diagnosis. The definitions and criteria of the World Health Classification of Tumors – Head and Neck Tumors book (1) (last updated in 2017), were used to diagnose the lesions. Randomized and controlled clinical trials, cohort studies, case-control studies, cross-sectional studies, case series, and case reports were included. Exclusion criteria were immunohistochemical studies, histomorphometric studies, radiological studies, genetic expression studies, histopathological studies, cytological studies, cell proliferation/apoptosis studies, *in vitro* studies, and review papers, unless any of these publication categories had reported any cases with enough clinical, radiological and histological information. Hybrid tumors containing parts of any of these lesions were not considered for this study, as they may behave differently from non-hybrid lesions. Ameloblastic sarcomatous lesions that presented hard tissue (ameloblastic fibrodentinosa sarcoma or ameloblastic fibro-odontosarcoma) were excluded.

Study selection

The titles and abstracts of all reports identified through the electronic searches were read independently by the authors. For studies appearing to meet the inclusion criteria, or for which there were insufficient data in the title and abstract to make a clear decision, the full report was obtained. Disagreements were solved by discussion between the authors. The clinical and radiological aspects, as well as the histological description of the lesions reported by the publications were thoroughly assessed by one of the authors (RSG), an expert in oral pathology, in order to confirm the diagnosis of AF or AFS.

Data extraction

The review authors independently extracted data using specially designed data extraction forms. Any disagreements were resolved by discussion. For each of the identified studies included, the following data were then extracted on a standard form, when available: year of publication, number of patients, patient's sex, age and race, follow-up period, duration of the lesion previously to treatment, lesion location (maxilla/mandible), anterior/posterior location (three categories: [a] anterior: lesions in the incisors/canine region; [b] premolar region; [c] posterior: lesions in the molars/retromolar region), recurrence, recurrence period, lesion size, presence of erosion of the subjacent cortical bone (for peripheral lesions), perforation of cortical bone, locularity radiological appearance (unilocular/multilocular), presence of radiopacities visible in the radiological exams, association of the lesion with a tooth (the tooth can either be erupted with the entire root(s) encompassed by the lesion or unerupted encompassing the entire tooth), tooth displacement and/or tooth root resorption due to lesion's growth, expansion of osseous region adjacent to the tumor, presence of clinical symptoms, and treatment performed (excision, curettage, fulguration, enucleation, partial resection, resection with continuity). For sarcomatous lesions, information on radiotherapy, chemotherapy, the number of recurrences, the occurrence of metastases, and the patient's death were also collected. AFS were defined as 'primary' or 'secondary' depending on whether they were *de novo* lesions or occurred after an AF, respectively. The lesion size was determined according to the largest diameter reported in the publications. Contact with authors for possible missing data was performed.

Analyses

The mean, standard deviation (SD), and percentages were presented as descriptive statistics. Kolmogorov–Smirnov test was performed to evaluate the normal distribution of the variables, and Levene's test evaluated homoscedasticity. The performed tests for two independent groups were

Student's t-test or Mann-Whitney test, depending on the normality. Pearson's chi-squared or Fisher's exact tests were used for categorical variables, depending on the expected count of events in a 2x2 contingency table. The probability of recurrence was calculated for several variables, in odds ratio (95% confidence interval). The degree of statistical significance was considered $p < 0.05$. All data were statistically analyzed using the Statistical Package for the Social Sciences (SPSS) version 23 software (SPSS Inc., Chicago, IL, USA).

RESULTS

Literature search

The study selection process is summarized in Figure 1. The search strategy in the databases resulted in 2,299 papers. Search in Google Scholar resulted in 46 eligible papers not found in the five main databases. A number of 756 articles were cited in more than one database (duplicates). The reviewers independently screened the abstracts for those articles related to the focus question. Of the resulted 1,589 studies, 1,268 were excluded for not being related to the topic or not presenting clinical cases. Additional hand-searching of journals and of the reference lists of selected studies yielded 28 additional papers. The full-text reports of the remaining 349 articles led to the exclusion of 105 because they did not meet the inclusion criteria (see Supplemental Appendix). The excluded studies did not have enough clinical, radiological and histological information to confirm a definite diagnosis of AF. Thus, a total of 244 publications were included in the review.

Description of the Studies and Analyses

244 publications were included in the present review (see Supplemental Appendix). Table 1 presents demographic and clinical features of all 279 central AF, 10 peripheral AF and 103 AFS. Of the 103 AFS, 71 were primary lesions and 25 secondary lesions occurring after the treatment of an

AF. There was not enough information in order to define whether an AFS was primary or secondary lesion in 7 cases.

Central AF and AFS were more prevalent in men than in women, and peripheral AF more prevalent in men. The mean age of the patients was higher in AFS than in central AF ($p<0.001$). Figure 2 shows the distribution of the central AF according to age, with a high prevalence on the first two decades of life. AFS had the highest prevalence on the second and third decades of life (Figure 3). The lesions were more prevalent in the mandible in comparison to the maxilla, and in the posterior region in comparison to the anterior region (figure 3 for central AF; figure 4 for AFS). Almost 80% of the central AF lesions showed bone expansion, and virtually all sarcomatous lesions presented with this clinical sign ($p<0.001$). Cortical bone perforation was present in 22.6% of the central AF and 90% in the sarcomatous lesions ($p<0.001$). Central AF less often caused clinical symptoms than AFS ($p<0.001$). AFS more often presented a multilocular radiological appearance than central AF. The percentage of root resorption was not different between AF and AFS. The mean lesion size of AFS was greater than for AF ($p<0.001$). 61.7% (111 out of 180 cases with information available) and 78.3% of the central AF (141/180) of the central AF cases were followed-up up to 3 and 5 years, respectively. With regard to AFS, 63.6% (49/77) and 81.8% (63/77) of the cases were followed-up up to 3 and 5 years, respectively.

AFS was far more often submitted to surgical resections, either marginal or segmental, than AF. About 19% of central AF recurred, versus 35% of the AFS ($p=0.004$). One case (12.5%) of peripheral AF recurred. 37 cases of central AF recurred only once, three cases recurred twice, one case 4 times, and one case presented 8 recurrences. Segmental resection resulted in the lowest rate of recurrence for most of the lesion types (Table 2). Central AF recurred for the first time after 50.1 ± 55.6 months (mean $\pm$ SD, min-max, 6-228; $n=38$). The mean $\pm$ SD time between the treatment of an AF and the occurrence of an AFS (secondary AFS) was 55.1 ± 54.7 (min-max, 3-168; $n=19$). Larger lesions and older patients were more often treated by surgical resections for central AF (Table 3).

16 AFS patients died from complications related to the lesion (21.1% - information was available for 76 cases). Three of these patients refused further treatment after some recurrences. There was information about the number of recurrences for 76 cases (considering recurrences for when an AFS was established – it does not consider the number of recurrences of AF, in case the AFS was secondary), of which 51 did not present recurrences (1 died), 7 subjects presented 1 recurrence (3 died), 9 individuals 2 recurrences (7 died), 3 patients 3 recurrences (2 died), 2 patients 4 recurrences (1 died), and 1 patient each with 6 and 8 recurrences (both died). For 2 patients (1 with 1 recurrence, 1 with 2 recurrences), there was no information about death. Patients submitted to chemo and radiotherapy had higher recurrence rates for AFS than those patients not submitted to the adjunctive therapies (Table 2). AFS recurred for the first time after a mean $\pm$ SD of 22.2 $\pm$ 39.6 months (min-max, 2-168; n=24). Nine and 20 patients (out of 73) with AFS were submitted to chemotherapy and radiotherapy, respectively, as adjunctive therapy. Three variables were statistically significant different between primary and secondary AFS: mean age of the patient, presence of dislocated/unerupted teeth due to the lesion growth, and the occurrence of metastases. Secondary AFS presented a higher recurrence rate than primary AFS (50% vs. 28.8%), even though the difference did not present statistical significance.

Table 4 shows the recurrence rate for central AF according to different factors. No factor showed to have a statistically significant effect on the recurrence rate. Table 5 shows the recurrence rate for AFS according to different factors. AFS treated by segmental resection had a 70.5% lower probability to recur (Odds Ratio 0.295; $p=0.049$) than when treated by marginal resection. Other factors did not seem to significantly affect the recurrence rate.

Table 6 shows the time of follow-up for different methods of treatment for central AF and AFS. Patients submitted to different treatments did not have a statistically significant difference in follow-up time for AF. With regard to AFS, patients submitted to curettage presented a statistically significant higher mean follow-up time than those patients submitted to marginal and segmental resection.

DISCUSSION

In the present literature review on AF and AFS many publications were excluded because they did not meet the inclusion criteria. This is not to say that all of them were not AF or AFS, but suggests that the authors perhaps need to better describe their findings and that many reviews included cases that may have the diagnosis questioned.

AF and AFS differed significantly with regard to bone expansion adjacent to the tumour, presence of clinical symptoms, cortical bone perforation, lesion mean size, mean age of the patients, and recurrence rates.

AFS more often presented as a multilocular radiolucency than central AF (52.3% vs. 39.4%). As patients with AFS presented at a higher mean age in compared to those with AF, together with the fact that more than 50% of reported cases had histologic documentation of AF in the same site (7), it was hypothesized that there is a stepwise malignant transformation (8). As AFS has an increased number and diversity of genetic alterations when compared to AF (9), this stepwise malignant transformation may be associated with chromosomal instability. There were more cases of displaced/retained teeth by primary AFS than by secondary AFS. This may be explained by the fact that many teeth were removed in surgery for AF. Therefore, fewer teeth are displaced or retained in the secondary AFS lesions.

Simple enucleation is related to a considerable recurrence rate for AF, a finding similar to that observed in keratocystic odontogenic tumors (10). As about 25% of AFS develop in a recurrent AF, some believe that AF is more aggressive than previously thought and more radical treatment is needed. The trend observed by the results of our review suggest that more conservative approaches were used for AF in young patients, and surgical resections were more often considered in older patients and when the tumour is large. More radical surgery should also be considered when the tumor recurs more than once (11, 12). Concerning the rate of secondary AFS observed here, the recurred and malignantly transformed cases of AF are more likely to be documented than ordinary

cases in the form of case reports (12). Therefore, it is possible that the rates of recurrence and malignant transformation found in our review are overestimated.

However, the vast majority (78.3%) of central AF cases were followed-up up to 5 years. Malignant transformation of AF can occur many years after the original diagnosis, and has been reported 10 (8, 13, 14), 12 (15), or 14 years (16) after the initial diagnosis. The mean time between the treatment of an AF and the occurrence of an AFS was 55.1 months. Hence, patients with a diagnosis of any tumours within the AF group should undergo have long-term follow-up, lifelong. An earlier diagnosis could reduce the risk of massive tumour extension resulting in devastating neurologic and cosmetic deformity (14). The gradual disappearance of the epithelium component in some recurrent AFS has been used for tumour staging, but the few number of cases reported is an important limiting factor. Further studies are necessary to confirm whether a dominant epithelial component is a good prognostic sign. It is interesting to note a case described by Takeda et al. (17), that noted several recurrences with increased malignancy, deposition of dentinoid material, but the epithelial component remained. The patient died by direct invasion.

Patients with AFS treated with chemotherapy and/or radiotherapy as adjunctive therapy had a higher recurrence rate than those who did not have these treatments, although these modalities are more commonly used in aggressive cases. AFS treated by segmental resection had a 70.5% lower chance of recurrence when treated by marginal resection. Therefore, segmental resection is still the most recommended treatment for AFS.

The results of our study have to be interpreted with caution because of its limitations. First, all included studies were retrospective reports, which inherently result in errors, with incomplete records. Secondly, many of the published cases had a short follow-up, which could have led to an underestimation of the actual recurrence rate. However, it is hard to define what it would be considered a short follow-up period to evaluate the recurrence of these lesions. Thirdly, many of the cases described were published as isolated case reports or small case series.

CONCLUSIONS

Very long follow-up is recommended for AF lesions, due to the risk of recurrence or malignant transformation into AFS. Segmental resection is the most recommended therapy for AFS.

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Declaration of conflicting interests

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FIGURE LEGENDS

Figure 1. Study screening process.

Figure 2. Distribution of central ameloblastic fibromas (n=279) according to age.

Figure 3. Distribution of ameloblastic fibrosarcomas according to age (for the cases which the patients' age were informed, n=102).

Figure 4. Topographical distribution of the known precise locations (n=233) of central ameloblastic fibromas. Cases involving multiple regions (or an entire quadrant) are indicated between arrows. Numbers at the top and bottom of the lines indicate cases involving both adjoining regions: anterior/premolar, premolar/molar. The asterisk (*) indicates the number of lesions from the anterior mandible or mandibular body that reached the angle and/or ramus. For the rest of the lesions (n=46), the location was the 'maxilla' (n=1), 'anterior maxilla' (n=1), 'posterior maxilla' (n=4), 'right maxilla' (n=1), 'mandible' (n=8), 'anterior mandible' (n=2), 'posterior mandible' (n=16), 'anterior and posterior mandible' (n=1), 'mandibular body' (n=4), 'left mandible' (n=1), 'right mandible' (n=1), 'angle/ramus' (n=1), 'left ramus' (n=1), and 'first and second deciduous molars' (n=1). The whole mandible was affected in 3 cases. The maxillary sinus was substantially affected in 16 lesions.

Figure 5. Topographical distribution of the known precise locations (n=70) of ameloblastic fibrosarcomas. Cases involving multiple regions (or an entire quadrant) are indicated between arrows. Numbers at the top and bottom of the lines indicate cases involving both adjoining regions: anterior/premolar, premolar/molar. The asterisk (*) indicates the number of lesions from the anterior mandible or mandibular body that reached the angle and/or ramus (n=33): 6 of these lesions anteriorly reached the incisors/canine area, 17 of these lesions anteriorly reached the premolars area, and 10 of these lesions anteriorly reached the molars area. For the rest of the lesions (n=33), the location was the 'left maxilla' (n=2), 'posterior maxilla' (n=3), 'right maxilla' (n=3), 'left maxillary sinus' (n=2), 'mandible' (n=1), 'paramedian mandible' (n=1), 'posterior mandible' (n=10), 'right mandible' (n=2), 'left mandible' (n=6), 'left masticator space' (n=1), 'middle face' (n=1). The whole maxilla was affected in 1 case. For some of these 33 cases without precise location, the lesions' extension varied considerably, and some cases extended to the floor of the mouth, soft and hard palate, pterygoid fossa and medial/lateral muscles/plates, epipharynx, nasopharynx, nasal cavity, nostril, ethmoidal bone, posterior ethmoidal cells, sphenoid sinuses, sphenoidal bone, infratemporal fossa, temporalis muscle, orbit, orbital part of the frontal bone, forehead, epidural space, skull base, anterior/middle cranial fossae, cavernous sinus, and basilar part of the occipital bone.

Table 1. Demographic and clinical features of ameloblastic fibromas (AF) and ameloblastic fibrosarcomas (AFS) described in the literature.

Variables	AF-peripheral	AF-central	AFS	<i>p</i> value ^a	AFS-primary ^b	AFS-secondary ^b	<i>p</i> value ^c
n	10	279	103		71	25	
Age (years), mean±SD (min-max)	12.0±18.9 (0-54; n=10)	15.2±11.3 (0-61; n=279)	27.7±15.6 (3-89; n=102)	<0.001 ^d	26.8±16.4 (3-89; n=70)	32.3±14.3 (12-77; n=25)	0.029 ^d
Men	5.0±3.0 (2-8; n=3)	16.2±11.4 (1-61; n=157)	29.2±15.7 (5-89; n=54)	<0.001 ^d	28.6±18.0 (5-89; n=36)	31.8±10.0 (16-48; n=15)	0.104 ^d
Women	15.0±22.3 (0-54; n=7)	14.5±11.2 (0-60; n=114)	26.3±15.5 (3-78; n=47)	<0.001 ^d	25.3±14.4 (3-78; n=33)	33.0±19.7 (12-77; n=10)	0.215 ^d
<i>p</i> value ^e	0.731	0.162	0.171		0.552	0.359	
Gender, n (%)							
Men	3 (30)	157 (57.9)	55 (53.9)	0.486 ^f	37 (52.9)	15 (60)	0.538 ^f
Women	7 (70)	114 (42.1)	47 (46.1)		33 (47.1)	10 (40)	
Unknown	0	8	1		1	0	
Jaw, n (%)							
Maxilla	6 (60)	57 (20.8)	24 (23.3)	0.599 ^f	18 (25.4)	5 (20)	0.590 ^f
Mandible	4 (40)	217 (79.2)	79 (76.7)		53 (74.6)	20 (80)	
Unknown	0	5	0		0	0	
Bone expansion, n (%)							
Yes	-	192 (78.4)	90 (97.8)	<0.001 ^f	66 (98.5)	23 (95.8)	0.460 ^g
No	-	53 (21.6)	2 (2.2)		1 (1.5)	1 (4.2)	
Unknown	-	34	11		4	1	
Symptomatic, n (%)							
Yes	0 (0)	38 (16.7)	32 (44.4)	<0.001 ^f	24 (42.1)	8 (53.3)	0.436 ^f
No	8 (100)	190 (83.3)	40 (55.6)		33 (57.9)	7 (46.7)	
Unknown	2	51	31		14	10	
Cortical bone perforation, n (%)							
Yes	1 (12.5)	44 (22.6)	73 (93.6)	<0.001 ^f	51 (91.1)	22 (100)	0.181 ^g
No	7 (87.5)	151 (77.4)	5 (6.4)		5 (8.9)	0	
Unknown	2	84	25		15	3	
Bone erosion, n (%) ^h							

Yes	1 (14.3)	-	-	-	-	-	
No	6 (85.7)	-	-	-	-	-	
Unknown	3	-	-	-	-	-	
Locularity, n (%)							
Unilocular	-	129 (60.6)	31 (47.7)	0.066 ^f	24 (49)	7 (43.8)	0.716 ^f
Multilocular	-	84 (39.4)	34 (52.3)		25 (51)	9 (56.3)	
Unknown	-	66	38		22	9	
Tooth displacement/ unerupted, n (%)							
Yes	2 (25)	152 (80.4)	35 (60.3)	0.002 ^f	33 (71.7)	2 (16.7)	0.001 ^g
No	6 (75)	37 (19.6)	23 (39.7)		13 (28.3)	10 (83.3)	
Unknown	2	90	45		25	13	
Tooth root resorption, n (%)							
Yes	0 (0)	39 (22.8)	15 (28.3)	0.414 ^f	10 (24.4)	5 (41.7)	0.208 ^g
No	8 (100)	132 (77.2)	38 (71.7)		31 (75.6)	7 (58.3)	
Unknown	2	108	50		30	13	
Treatment, n (%)							
None	0	0	1 (1.1)		0	1 (4)	
Excision	9 (100)	0	0		0	0	
Curettage	0	6 (2.5)	3 (3.3)		2 (3.0)	1 (4)	
Enucleation	0	192 (79.0)	4 (4.3)		3 (4.6)	0	
Marginal resection	0	19 (7.8)	16 (17.4)		12 (18.2)	4 (16)	
Segmental resection ⁱ	0	26 (10.7)	65 (70.7)		46 (69.7)	19 (76)	
Chemotherapy only	0	0	1 (1.1)		1 (1.5)	0	
Fulguration	0	0	2 (2.1)		2 (3.0)	0	
Unknown	1	36	11		5	0	
Adjunctive therapy, n (%) ^j							
Chemotherapy							
Yes	-	-	9 (12.3)		6 (10.7)	3 (18.8)	0.317 ^g
No	-	-	64 (87.7)		50 (89.3)	13 (81.2)	
Unknown	-	-	30		15	9	

Radiotherapy							
Yes	-	-	20 (27.4)		15 (26.8)	5 (31.2)	0.475 ^g
No	-	-	53 (72.6)		41 (73.2)	11 (68.8)	
Unknown	-	-	30		15	9	
Metastasis, n (%) ^j							
Yes	-	-	7 (9)		2 (3.4)	4 (21.1)	0.030 ^g
No	-	-	71 (91)		56 (96.6)	15 (78.9)	
Unknown	-	-	25		13	6	
Death, n (%) ^j							
Yes	-	-	16 (21.1)		10 (18.2)	5 (26.3)	0.325 ^g
No	-	-	60 (78.9)		45 (81.8)	14 (73.7)	
Unknown	-	-	27		16	6	
Recurrence, n (%)							
Yes	1 (12.5)	42 (19.2)	28 (34.6)	0.005 ^f	17 (28.8)	10 (50)	0.084 ^f
No	7 (87.5)	177 (80.8)	53 (65.4)		42 (71.2)	10 (50)	
Unknown	2	60	22		12	5	
Follow-up time (months), mean±SD (min-max)	34.3±41.1 (8-120; n=7)	47.7±60.5 (1-408; n=180)	44.8±57.2 (1-360; n=77)	0.553 ^d	46.7±62.0 (1-360; n=57)	38.8±43.0 (1-192; n=19)	0.957 ^d
Lesion size (cm), mean±SD (min-max)	1.0±0.5 (0.5-2.0; n=9)	4.8±4.7 (0.3-50.5; n=178)	7.0±4.7 (1.8-30.0; n=45)	<0.001 ^d	6.7±3.5 (1.8-15.0; n=34)	7.9±7.6 (2.5-30.0; n=11)	0.905 ^d

SD – standard deviation, AFS-primary - ameloblastic fibrosarcoma as primary lesion, AFS-secondary - ameloblastic fibrosarcoma occurring after an ameloblastic fibroma

^a Comparison between AF-central and AFS

^b There was not enough information in order to define whether an AFS was primary or secondary in 7 lesions

^c Comparison between AFS-primary and AFS-secondary

^d Mann-Whitney test

^e Comparison of the mean age between men and women (Mann-Whitney test)

^f Pearson chi-squared test

^g Fisher's exact test

^h Peripheral lesions only

ⁱ Resection with continuity defect

^j For sarcomas only

Table 2. Treatment recurrence – for the lesions with available information about treatment and recurrence.

Treatment Recurrence/total (% recurrence)	AF-peripheral	AF-central	AFS	AFS-primary	AFS-secondary
Excision	1/8 (12.5)	-	-	-	-
Curettage	-	2/6 (33.3)	3/3 (100)	2/2 (100)	1/1 (100)
Enucleation	-	34/167 (20.4)	2/2 (100)	1/1 (100)	-
Marginal resection	-	4/18 (22.2)	7/14 (50)	6/11 (54.5)	1/3 (33.3)
Segmental resection ^a	-	1/16 (6.3)	13/57 (22.8)	5/41 (12.2)	8/16 (50)
Fulguration	-	-	2/2 (100)	2/2 (100)	-
Total	1/8 (12.5)	41/207 (19.8)	27/78 (34.6)	16/57 (28.1)	10/20 (50)
Adjunctive therapy					
Chemotherapy					
Yes	-	-	4/8 (50)	2/5 (40)	2/3 (66.7)
No	-	-	17/60 (28.3)	13/48 (27.1)	3/11 (27.3)
Radiotherapy					
Yes	-	-	9/19 (47.4)	7/14 (50)	2/5 (40)
No	-	-	12/49 (24.5)	8/39 (20.5)	3/9 (33.3)

AF – ameloblastic fibroma, AFS - ameloblastic fibrosarcoma, AFS-primary - ameloblastic fibrosarcoma as primary lesion, AFS-secondary - ameloblastic fibrosarcoma occurring after an ameloblastic fibroma

^a Resection with continuity defect

Table 3. Lesion size and patient's age for patients presenting central ameloblastic fibromas, according to different treatments – for the lesions with available information about both recurrence and the factors here included.

Treatment	Lesion size (cm) Mean±SD (min-max; n)	<i>p</i> value ^{b,c}	Patient age (years) Mean±SD (min-max; n)	<i>p</i> value ^{b,c}
1. Curettage	4.0 (n=1)		16.2±7.0 (10-27; n=6)	
2. Enucleation	3.8±2.3 (0.3-11.0, n=126)	(1-2) 0.803 (1-3) 0.857 (1-4) 0.261	13.0±9.2 (0-47; n=192)	(1-2) 0.184 (1-3) 0.069 (1-4) 0.119
3. Marginal resection	5.1±2.3 (2.0-10.0; n=13)	(2-3) 0.038 (2-4) <0.001	28.7±16.9 (3-60; n=19)	(2-3) <0.001 (2-4) <0.001
4. Segmental resection ^a	11.2±9.8 (3.0-50.5; n=22)	(3-4) 0.002	23.5±11.6 (4-48; n=26)	(3-4) 0.363

^a Resection with continuity defect

^b Mann-Whitney test

^c Comparison of the difference in lesion size or patient age between the different methods of treatment. The methods of treatment are identified by numbers, according to the first column of the table

Table 4. Recurrence rate for central ameloblastic fibromas (primary lesions only) according to different factors – for the lesions with available information about both recurrence and the factors here included.

Factor	Recurrence/total (% recurrence)	<i>p</i> value	Odds ratio (95% CI)	<i>p</i> value
<i>Treatment</i>				
Curettage	2/6 (33.3)	0.365 ^{a,d}	0.511 (0.090, 2.909) ^j	0.450
Enucleation	34/167 (20.4)	0.480 ^{a,e}	0.571 (0.075, 4.345) ^k	0.589
Marginal resection	4/18 (22.2)	0.169 ^{a,f}	0.133 (0.009, 1.872) ^l	0.135
Segmental resection ^c	1/16 (6.3)	0.528 ^{a,g}	1.118 (0.346, 3.613) ^m	0.853
		0.148 ^{a,h}	0.261 (0.033, 2.044) ⁿ	0.201
		0.207 ^{a,i}	0.233 (0.023, 2.349) ^o	0.217
<i>Jaw</i>				
Maxilla	5/41 (12.2)	0.188 ^b	1	0.194
Mandible	37/174 (21.3)		1.945 (0.713, 5.304)	
<i>Bone expansion</i>				
No	4/42 (9.5)	0.055 ^b	1	0.064
Yes	35/153 (22.9)		2.818 (0.941, 8.441)	
<i>Cortical bone perforation</i>				
No	18/126 (14.3)	0.626 ^b	1	0.627
Yes	6/34 (17.6)		1.286 (0.467, 3.541)	
<i>Locularity</i>				
Unilocular	13/99 (13.1)	0.502 ^b	1	0.503
Multilocular	11/65 (16.9)		1.348 (0.563, 3.223)	
<i>Tooth root resorption</i>				
No	20/114 (17.5)	0.126 ^a	1	0.172
Yes	2/29 (6.9)		0.348 (0.077, 1.584)	

CI - confidence interval

^a Fisher's exact test

^b Pearson's chi-squared test

^c Resection with continuity defect

^d Significance of the difference of the recurrence rate between curettage and enucleation

^e Significance of the difference of the recurrence rate between curettage and marginal resection

^f Significance of the difference of the recurrence rate between curettage and segmental resection

^g Significance of the difference of the recurrence rate between enucleation and marginal resection

^h Significance of the difference of the recurrence rate between enucleation and segmental resection

ⁱ Significance of the difference of the recurrence rate between marginal resection and segmental resection

^j Odds ratio of the recurrence probability of enucleation in relation to curettage

^k Odds ratio of the recurrence probability of marginal resection in relation to curettage

^l Odds ratio of the recurrence probability of segmental resection in relation to curettage

^m Odds ratio of the recurrence probability of marginal resection in relation to enucleation

ⁿ Odds ratio of the recurrence probability of segmental resection in relation to enucleation

^o Odds ratio of the recurrence probability of segmental resection in relation to marginal resection

Table 5. Recurrence rate for ameloblastic fibrosarcomas according to different factors – for the lesions with available information about both recurrence and the factors here included.

Factor	Recurrence/total (% recurrence)	<i>p</i> value	Odds ratio (95% CI)	<i>p</i> value
<i>Treatment</i>				
Curettage	3/3 (100)	0.176 ^{a,d}	-	-
Enucleation	2/2 (100)	0.300 ^{a,e}	-	-
Fulguration	2/2 (100)	0.016 ^{a,f}	-	-
Marginal resection	7/14 (50)	0.061 ^{a,g}	1	
Segmental resection ^c	13/57 (22.8)	0.049 ^{a,h}	0.295 (0.088, 0.997) ⁱ	0.049
<i>Jaw</i>				
Maxilla	7/18 (38.9)	0.694 ^b	1	0.695
Mandible	21/62 (33.9)		0.805 (0.272, 2.379)	
<i>Bone expansion</i>				
No	1/2 (50)	0.570 ^a	1	0.639
Yes	25/74 (33.8)		0.510 (0.031, 8.503)	
<i>Cortical bone perforation</i>				
No	1/5 (20)	0.425 ^a	1	0.479
Yes	22/61 (36.1)		2.256 (0.237, 21.467)	
<i>Locularity</i>				
Unilocular	10/27 (37)	0.334 ^b	1	0.337
Multilocular	7/28 (25)		0.567 (0.178, 1.805)	
<i>Tooth root resorption</i>				
No	9/34 (26.5)	0.187 ^a	1	0.217
Yes	1/12 (8.3)		0.253 (0.028, 2.244)	
<i>Occurring after an ameloblastic fibroma?</i>				
No	17/59 (28.8)	0.084 ^b	1	0.089
Yes	10/20 (50)		2.471 (0.872, 7.004)	

CI - confidence interval

^a Fisher's exact test

^b Pearson's chi-squared test

^c Resection with continuity defect

^d Significance of the difference of the recurrence rate between marginal resection and curettage

- ^e Significance of the difference of the recurrence rate between marginal resection and enucleation (or fulguration)
- ^f Significance of the difference of the recurrence rate between segmental resection and curettage
- ^g Significance of the difference of the recurrence rate between segmental resection and enucleation (or fulguration)
- ^h Significance of the difference of the recurrence rate between marginal resection and segmental resection
- ⁱ Odds ratio of the recurrence probability of segmental resection in relation to marginal resection

Table 6. Time of follow-up for different methods of treatment for central ameloblastic fibromas and ameloblastic fibrosarcomas.

Treatment	Time of follow-up Mean±SD (min-max; n)	<i>p</i> value ^{b,c}
AF-central		
1. Curettage	43.3±66.5 (1-120; n=3)	(1-2) 0.420 (1-3) 0.313 (1-4) 0.527
2. Enucleation	44.6±51.4 (2-384; n=146)	(2-3) 0.169 (2-4) 0.073
3. Marginal resection	93.3±114.8 (6-408; n=17)	(3-4) 0.067
4. Segmental resection ^a	25.0±24.2 (2-84; n=14)	
AFS		
1. Curettage	224.0±123.2 (120-360; n=3)	(1-2) 0.083 (1-3) 0.248 (1-4) 0.015 (1-5) 0.004
2. Enucleation	81.5±48.8 (47-116; n=2)	(2-3) 1.000 (2-4) 0.233 (2-5) 0.077
3. Fulguration	105.0±106.1 (30.180; n=2)	(3-4) 0.233 (3-5) 0.164
4. Marginal resection	42.8±51.5 (1-216; n=15)	(4-5) 0.351
5. Segmental resection ^a	32.6±31.2 (2-144; n=54)	

SD – standard deviation, AF-central - central ameloblastic fibromas, AFS - ameloblastic fibrosarcomas

^a Resection with continuity defect

^b Mann-Whitney test

^c Comparison of the difference in mean follow-up time between the different methods of treatment.

The methods of treatment are identified by numbers, according to the first column of the table