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SUPPLEMENTAL APPENDIX

- a. Materials and Methods: search strategies, study selection, data extraction
- b. Additional figure;
- c. Additional table;
- d. Publications included in the review;
- e. Publications excluded for not having enough clinical, radiological and histological information;
- f. Publications excluded due to the possibility of duplicated cases.
- g. PRISMA checklist

a. Materials and Methods

Search strategies

An electronic search without time restrictions was undertaken in February 2018 in the following databases: PubMed/Medline, Web of Science, Science Direct, J-Stage, and Lilacs. The following terms were used in the search strategies:

("central giant cell lesion") OR ("central giant cell reparative granuloma") OR ("central giant cell granuloma") OR ("central giant cell") NOT ("elastolytic giant cell granuloma")

Google Scholar and Crossref were also checked. A manual search of related journals, including *Acta Odontologica Scandinavica*, *Acta Oto-Laryngologica*, *Annals of Otology Rhinology and Laryngology*, *British Journal of Oral and Maxillofacial Surgery*, *Cancer, Head & Neck*, *Head and Neck Pathology*, *International Journal of Oral and Maxillofacial Surgery*, *Japanese Journal of Oral and Maxillofacial Surgery*, *Journal of Dental Research*, *Journal of Craniofacial Surgery*, *Journal of Cranio-Maxillofacial Surgery*, *Journal of Japanese Society of Oral Oncology*, *Journal of the Japanese Stomatological Society*, *Journal of Laryngology and Otology*, *Journal of Maxillofacial and Oral Surgery*, *Journal of Nihon University School of Dentistry*, *Journal of Oral and Maxillofacial Surgery*, *Journal of Oral Pathology and Medicine*, *Journal of the Stomatological Society*, *Laryngoscope*, *Oral Diseases*, *Oral Oncology*, *Oral Surgery Oral Medicine Oral Pathology Oral Radiology*, *Otolaryngology -- Head and Neck Surgery*, and *Quintessence International*, was performed. The reference list of the 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 CGCL, even not having the term “central giant cell lesion” in the title of the article, were also re-evaluated by an author of the present study.

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 resolved 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 (R.S.G.) of the present study, in order to confirm the diagnosis of CGCL.

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, for how long the lesion has been noticed before initial 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), lesion size, perforation of cortical bone, locularity appearance in radiological exams (unilocular/multilocular), presence of radiopacities visible in the radiological exams, association of the lesion with a 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, classification in aggressive or non-aggressive lesion (see sub-item *Analyses*), treatment performed (curettage, debulking, enucleation, partial resection, resection with continuity, chemotherapy, radiotherapy, corticoid, calcitonin, interferon, monoclonal antibody, bisphosphonate), performance of curettage or peripheral osteotomy right after surgical excision, number of treatment steps, recurrence, recurrence period, number of recurrences, occurrence of spontaneous resolution, and blood exams (alkaline phosphatase, parathormone, calcium, phosphate). The lesion size was determined according to the largest diameter reported in the publications. Contact with authors for possible missing data was performed.

b. Additional figure

Figure S1. Study screening process.

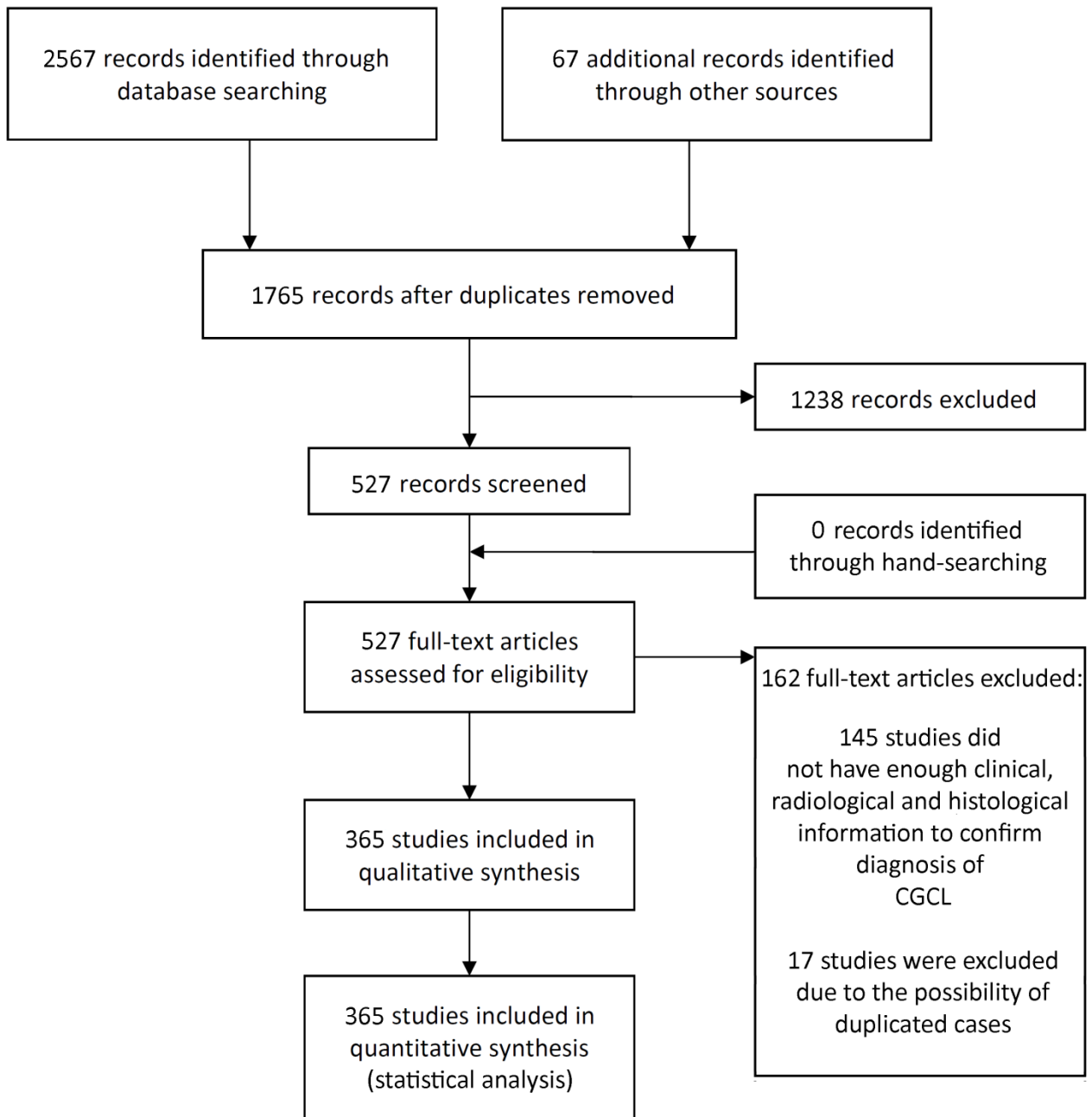


Table S1. Type of first treatment performed in lesions of different size ranges - for the lesions with available information about both treatment and size.

Size (cm)	Curettage	Enucleation	Marginal resection	Segmental resection ^a	Drug therapy ^b	Debulking or radiotherapy	Total
0-2.0	46 (48.4)	20 (21.1)	2 (2.1)	3 (3.1)	24 (25.3)	0 (0)	95 (100)
2.1-4.0	109 (41.1)	74 (27.9)	16 (6.1)	14 (5.3)	49 (18.5)	3 (1.1)	265 (100)
4.1-6.0	61 (35.7)	39 (22.8)	19 (11.1)	20 (11.7)	30 (17.5)	2 (1.2)	171 (100)
>6.0	33 (44.6)	8 (10.8)	9 (12.1)	13 (17.6)	11 (14.9)	0 (0)	74 (100)

^a Resection with continuity defect

^b Therapy with a drug, which can be either corticoid, calcitonin, or monoclonal antibody

d. Publications included in the review

The 365 publications included in the review are listed below.

1. Abdo EN, Alves LC, Rodrigues AS, Mesquita RA, Gomez RS. Treatment of a central giant cell granuloma with intralesional corticosteroid. *Br J Oral Maxillofac Surg.* 2005 Feb;43(1):74-6.
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e. Publications excluded for not having enough clinical, radiological and histological information

The following excluded studies did not have enough clinical, radiological and histological information to confirm the diagnosis of central giant cell granuloma. The list also includes publications identified by other authors as presenting cases of these lesions, but which did not fulfill the inclusion criteria, as well as hybrid tumors containing parts of CGCG and a number of conditions that can present with lesions that histologically are indistinguishable from the CGCG (listed in the sub-item ***Inclusion and Exclusion Criteria*** of the text).

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f. Publications excluded due to the possibility of duplicated cases

The following studies were excluded due to the possibility of duplicated cases, usually originated from clinical series from the same service or University.

1. Amaral FR, Bernardes VF, Duarte AP, Pereira NB, Vasconcelos AC, Gomez RS, Gomes CC. Quantitative expression analysis of apoptotic/antiapoptotic genes and association with immunolocalization of BAX and BCL-2 in peripheral and central giant cell lesions of the jaws. *Tumour Biol*. 2011 Oct;32(5):997-1003.
2. Amaral FR, Gomes CC, Oliveira CS, Souza PEA, Gomez RS. Clonality analysis of giant cell lesions of the jaws. *Braz. dent. j* 2010;21(4):361-364.
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6. Moghadam SA, Ghorbanpour M. Central Giant Cell Granuloma of the Jaws: Correlation between Vascularity and Biologic Behavior. *J Dent Mater Tech* 2017;6(1):35-39.
7. Nogueira RL, Faria MH, Osterne RL, Cavalcante RB, Ribeiro RA, Rabenhorst SH. Glucocorticoid and calcitonin receptor expression in central giant cell lesions: implications for therapy. *Int J Oral Maxillofac Surg*. 2012 Aug;41(8):994-1000.
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14. Vered M, Buchner A, Dayan D. Giant cell granuloma of the jaw bones--a proliferative vascular lesion? Immunohistochemical study with vascular endothelial growth factor and basic fibroblast growth factor. *J Oral Pathol Med.* 2006 Nov;35(10):613-9.
15. Vered M, Buchner A, Dayan D. Immunohistochemical expression of glucocorticoid and calcitonin receptors as a tool for selecting therapeutic approach in central giant cell granuloma of the jawbones. *Int J Oral Maxillofac Surg.* 2006 Aug;35(8):756-60.
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17. Whitaker SB, Bouquot JE. Estrogen and progesterone receptor status of central giant cell lesions of the jaws. *Oral Surg Oral Med Oral Pathol.* 1994 Jun;77(6):641-4.

g. PRISMA checklist



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Introduction
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Introduction
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Inclusion and Exclusion Criteria
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Search strategies
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Search strategies
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Study selection
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Data extraction
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Data extraction
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Data extraction and analyses
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Data extraction and analyses

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Data extraction and analyses
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Data extraction and analyses
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Literature search Figure S1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Description of the Studies Tables 1-4
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not performed
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Discussion
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Discussion
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Conclusion
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Acknowledgements

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