



REVIEW ARTICLE

LATERAL PERIODONTAL CYST AND ITS BOTRYOID VARIANT: A NARRATIVE REVIEW WITH AN ILLUSTRATIVE CASE AND A PROPOSED DIAGNOSTIC AND THERAPEUTIC ALGORITHM

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Abstract

Background: The lateral periodontal cyst (LPC) and its multilocular botryoid variant, the botryoid odontogenic cyst (BOC), are uncommon developmental odontogenic cysts arising along the lateral root surface of vital teeth. Their well-defined interradicular radiolucency overlaps with inflammatory lesions and with cysts of higher recurrence potential, notably the odontogenic keratocyst and the glandular odontogenic cyst, making misdiagnosis a recognised problem. This article reviews their clinical, radiographic and histopathological features and proposes a decision-support framework.

Materials and Methods: This is a narrative review with a targeted narrative update, not an independently conducted systematic review: no de novo screening, risk-of-bias appraisal or quantitative synthesis was performed by the authors. All aggregated epidemiological, treatment and recurrence figures are as published by Chrcanovic and Gomez (July 2017 search; 146 publications). A targeted, non-systematic update in PubMed/MEDLINE, Web of Science and Scopus supplied representative publications, selected narratively. One illustrative case treated by enucleation with guided bone regeneration is reported.

Results: In the published aggregated dataset, BOC differed from LPC by larger mean size (2.8 versus 1.0 cm), more frequent mandibular location (85.3% versus 69.8%), more frequent multilocularity (46.1% versus 1.5%) and higher reported recurrence (21.7% versus 2.4%). Enucleation was the technique most often reported for LPC; evidence on regenerative adjuncts is confined to case reports and small series. In the illustrative case, healing was uneventful, with no recurrence at 12 months and histopathological confirmation.

Conclusions: Histopathological examination remains indispensable, because clinical and radiographic features alone cannot exclude lesions of higher recurrence potential. The aggregated data support a higher recurrence frequency for BOC and justify prolonged surveillance, but derive from heterogeneous case-level literature and require cautious interpretation. The proposed algorithm has not been externally validated.

Keywords: Lateral periodontal cyst; Botryoid odontogenic cyst; Odontogenic cysts; Differential diagnosis; Surgical enucleation; Guided bone regeneration; Recurrence.

INTRODUCTION

The cysts of the jaws comprise odontogenic and non-odontogenic entities whose biological behaviour ranges from indolent to locally aggressive, and whose treatment and follow-up requirements differ accordingly^{1,2,3,4}. Among the developmental odontogenic cysts, the lateral periodontal cyst (LPC) is an uncommon, non-inflammatory lesion that develops along the lateral root surface of a vital tooth, most frequently in the mandibular canine and premolar region^{5,6,7,8}. Its polycystic counterpart, the botryoid odontogenic cyst (BOC), was described by

Weathers and Waldron as a multilocular, grape-like lesion and is currently regarded as a variant of the same entity rather than a separate disease^{9,10}.

In the fifth edition (2022) of the World Health Organization (WHO) Classification of Head and Neck Tumours, the category "lateral periodontal cyst/botryoid odontogenic cyst" is explicitly recognised. Its essential diagnostic criteria are a lateral or interradicular location adjacent to a vital tooth and a thin, non-keratinised epithelial lining bearing characteristic focal "whorled" plaques; multilocular examples correspond to the

The largest aggregated analysis of published cases is the systematic review of Chrcanovic and Gomez¹². In that dataset, LPC occurred at a mean age of approximately 46.8 years, showed a mandibular predominance (approximately 69.8%), was unilocular in 98.5% of cases with recorded locularity and had a mean size of about 1.0 cm. BOC was more frequently mandibular (approximately 85.3%), multilocular in about 46.1% of documented cases and larger (mean approximately 2.8 cm), with longer reported follow-up and a higher recurrence frequency (Section 3.1). These figures are reproduced here as published by those authors; they were not recalculated for the present article.

Diagnostically, LPC is usually asymptomatic and detected incidentally during routine radiographic examination. The adjacent teeth generally remain vital, and the lesion appears as a well-circumscribed, round or tear-drop-shaped radiolucency with a corticated margin along the lateral aspect of the root (Figure 1). This appearance overlaps with inflammatory endodontic lesions and with odontogenic cysts and tumours of more aggressive behaviour, so that histopathological examination is required for a definitive diagnosis^{1,2,3,5,6,13,14}.

The clinical relevance of this overlap is supported by retrospective biopsy-service data, in which a substantial proportion of lesions submitted with a clinical diagnosis of LPC were ultimately reported as inflammatory cysts or as odontogenic keratocyst (OKC)^{2,15,16}. Golob Deeb et al. specifically documented that, among premolar and anterior tooth-bearing radiolucencies clinically interpreted as LPC, a substantial number proved histologically to be OKC¹⁷. A lateral radiolucency that is radiographically "compatible" with LPC therefore does not exclude entities with a substantially higher recurrence potential, such as OKC or the glandular odontogenic cyst (GOC)^{3,5,13,16}.

Against this background, the present article aims to (i) summarise the clinical, radiographic and histopathological features that distinguish LPC and BOC from their principal differential diagnoses; (ii) review the reported surgical and regenerative management options and the recurrence figures associated with them, while making the provenance of every quantitative value explicit; (iii) present one illustrative case managed by enucleation with guided bone regeneration (GBR); and (iv) propose a decision-support framework for lateral and interradicular radiolucencies. These aims are addressed in Sections 3 and 4. The framework presented in Section 4.2 is an author-developed clinical synthesis and has not been externally validated.

Review Design

This article is a narrative review incorporating a targeted narrative update of the more recent literature and one illustrative clinical case. It is not an independently conducted systematic review. No de novo systematic screening of the literature, no duplicate independent study selection, no formal risk-of-bias or certainty-of-evidence appraisal, and no meta-analysis or other quantitative synthesis were performed by the present authors.

For the same reason, no PRISMA flow diagram is presented. Reproducing the flow diagram of the reference systematic review would risk suggesting that the screening process had been carried out for this article, which is not the case; the screening yield of that review is therefore described narratively in Section 2.2 and attributed explicitly to its authors. This solution avoids any ambiguity about the provenance of the evidence and is consistent with the reporting expectations for a narrative review.

Throughout the manuscript the provenance of each statement is made explicit. Aggregated quantitative data are identified as derived from the reference systematic review¹²; qualitative statements arising from the targeted narrative update are identified as such; and observations relating to the illustrative case are confined to Section 3.5.

Reference Systematic Review as the Source of Quantitative Data

The quantitative evidence presented in this manuscript — age, anatomical distribution, lesion size, locularity, root resorption, follow-up duration, distribution of surgical techniques and recurrence — was derived from the previously published systematic review by Chrcanovic and Gomez¹². No independent systematic screening or quantitative re-analysis was undertaken for the present narrative review. As reported by those authors, that review followed PRISMA reporting guidance and was based on an electronic search performed in July 2017 without temporal restriction, with eligibility limited to publications containing sufficient clinical, radiographic and histopathological information to confirm the diagnosis. The authors of that review reported the inclusion of 146 publications, comprising 157 gingival cysts of the adult (GCA), 213 LPCs and 96 BOCs¹². Neither the screening process nor the exclusion of records was performed by the present authors, and the targeted narrative update described below did not modify the underlying dataset.

Targeted Narrative Update

To extend the discussion beyond the search date of the reference systematic review, a targeted, non-systematic update of the literature was carried out in PubMed/MEDLINE, Web of Science and Scopus, using the concepts "lateral periodontal cyst", "botryoid odontogenic cyst", "odontogenic cyst" and "guided bone regeneration". Particular attention was given to cone-beam computed tomography (CBCT), to regenerative surgical adjuncts, and to reports of clinical and radiographic misdiagnosis.

Publications were selected narratively by the authors as representative of these themes. No systematic screening, duplicate selection, formal eligibility assessment or quantitative synthesis was performed, and no meta-analysis was undertaken. The number of records retrieved was not recorded, and the update is therefore not reproducible in the sense required of a systematic review; it is intended solely to integrate recent evidence qualitatively.

Selection of Representative Literature

Preference was given to publications that concerned LPC or BOC (or, for the regenerative section, guided bone regeneration in intraosseous or interradicular defects); reported a histopathologically confirmed diagnosis; described the clinical and radiographic findings, the treatment performed and the follow-up; and were available in full text. Publications lacking histopathological confirmation, describing hybrid or unclassifiable histopathological features, or available only as conference abstracts without accessible full text were not used as sources of clinical evidence. Textbooks, classification documents and previous reviews were cited for background, terminology and diagnostic criteria. Publications in English were considered.

These preferences describe how representative literature was chosen for a narrative synthesis; they do not constitute a systematic eligibility assessment, and no record of excluded publications was kept.

Illustrative Clinical Case

One clinical case, managed by enucleation with guided bone regeneration, is reported to illustrate the diagnostic and therapeutic sequence discussed in this review. Documentation comprised clinical photographs, panoramic radiography, CBCT and histopathological examination of the enucleated specimen. Written informed consent for the publication of clinical data and images was obtained from the patient. The case is presented for illustrative purposes only; a single case provides no comparative

or generalisable evidence and is not used to support any of the quantitative statements in this article.

Development of the Proposed Algorithm

The proposed algorithm (Figure 7) is an author-developed clinical synthesis based on the reviewed literature and the diagnostic principles outlined in the 2022 WHO Classification¹¹. It has not been externally validated and should therefore be considered a decision-support framework rather than a validated clinical pathway. No formal consensus method (such as a Delphi process), no external expert panel and no prospective evaluation were used in its construction, and none of its elements should be interpreted as a formally graded recommendation.

Terminology, Units and Statistical Analysis

No statistical analysis was performed for the present article. Every numerical value reported is either a figure published in the reference systematic review¹² or a descriptive measurement recorded for the illustrative case; no pooling, re-estimation or hypothesis testing was undertaken, and no measure of uncertainty is reported beyond those published in the original source. Measurements are expressed in International System (SI) units. Individual teeth are designated according to the two-digit FDI notation. Abbreviations are defined at first use and listed at the end of the manuscript.

RESULTS

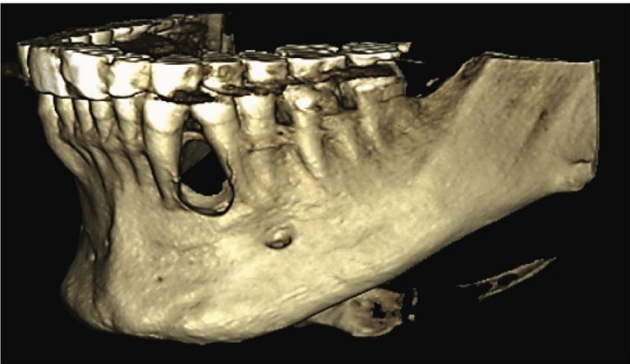
Clinical and Radiographic Features of LPC and BOC

Although LPC and BOC share a common developmental origin and overlapping histological features, the aggregated published data indicate that they differ in lesion size, frequency of multilocularity and reported recurrence — variables that bear directly on therapeutic decision-making and on the duration of follow-up¹².

LPC typically presents as a small, asymptomatic, well-corticated radiolucency situated between the roots of vital teeth, most often in the mandibular canine–premolar region (Figure 1a). Larger lesions may thin or perforate the cortical plates, which is best appreciated on CBCT (Figure 1b)^{6,7,18}. Multifocal presentations have been described but are rare¹⁹. BOC, by contrast, is more often multilocular and larger, and its lobulated architecture may produce a scalloped or "grape-like" radiographic outline^{9,10,20}.



(a)



(b)

Figure 1. Radiographic and three-dimensional appearance of a lateral periodontal cyst. (a) Panoramic radiograph showing a well-circumscribed radiolucency with a sclerotic border between the roots of teeth 33 and 34, with root displacement.

(b) Three-dimensional reconstruction from cone-beam computed tomography of the left mandible showing the cystic lesion between the roots of teeth 33 and 34, with loss of the buccal and lingual cortical plates. Both panels are reproduced from Ramalingam et al.¹⁸, distributed under the terms of the Creative Commons Attribution 4.0 International (CC BY 4.0) licence, which permits reuse provided the original source is credited. These images do not relate to the illustrative case reported in Section 3.5

The parameters summarised in Table 1 are reported as published in the reference systematic review¹². Percentages refer only to those cases in which the specific variable was documented, because many of the underlying publications provided incomplete clinical records; the denominators therefore vary between rows.

Table 1. Comparative parameters of lateral periodontal cyst and botryoid odontogenic cyst, reported as published in the reference systematic review¹². Values are means ± standard deviation or percentages of cases in which the variable was documented.

Variable	LPC	BOC	Clinical implication
Mean age (years)	46.8 ± 12.5	54.0 ± 15.7	BOC tends to present later in life
Mandibular location	69.8%	85.3%	BOC more frequently mandibular
Multilocular pattern (cases with recorded locularity)	1.5%	46.1%	Multilocularity should raise suspicion of BOC and of other multilocular lesions
Mean size (cm)	1.0 ± 0.6	2.8 ± 2.8	BOC lesions are larger; critical-sized bone defects are more likely
Root resorption (reported cases)	3.8%	6.3%	Uncommon but possible; relevant to differential diagnosis
Mean follow-up (months)	15.2 ± 16.3	34.3 ± 42.9	Reported surveillance has been longer for BOC
Reported recurrence	2.4%	21.7%	Principal determinant of adjuvant management and follow-up duration in BOC

The wide standard deviations, particularly for BOC size and follow-up duration, reflect substantial heterogeneity between the source publications and should be borne in mind when these values are applied to individual patients.

Histopathological Features and Differential Diagnosis

Histopathological examination is the only means of establishing a definitive diagnosis. LPC is lined by a thin, non-keratinised squamous or cuboidal epithelium, generally one to five cell layers thick, in which focal nodular thickenings — the characteristic "whorled" or plaque-like proliferations, frequently containing glycogen-rich clear cells — are the diagnostic hallmark^{5,8,11}. The epithelial–connective tissue interface is flat and the basal layer is not palisaded. BOC shows the same epithelial features but in a multicystic architecture, with several small cystic compartments separated by thin fibrous septa; this polycystic configuration, rather than any cytological difference, defines the variant^{9,10,20}.

The two principal differential diagnoses among developmental odontogenic cysts are OKC and GOC, both of which carry a considerably higher recurrence potential. OKC is characterised by a uniform parakeratinised squamous lining of five to eight cell layers with a corrugated luminal surface and a palisaded, hyperchromatic basal layer^{3,21}. GOC is defined by a combination of features rather than by any single criterion, including surface hobnail cells, intraepithelial microcysts or duct-like spaces, mucous cells, epithelial spheres and

occasional cilia²². Because the plaque-like thickenings of LPC and BOC may be focal and easily missed in a limited sample, complete submission of the enucleated specimen for histopathological examination is preferable to incisional sampling whenever the lesion can be removed in its entirety^{1,3}.

The principal discriminating features are summarised in Table 3. Inflammatory lesions of endodontic origin — the lateral radicular cyst and the apical granuloma — remain the most frequent clinical mimics and are distinguished primarily by loss of pulp vitality in the adjacent tooth^{16,23,24}.

Table 3. Principal histopathological and clinical features distinguishing lateral periodontal cyst (LPC) and botryoid odontogenic cyst (BOC) from their main differential diagnoses. The table summarises established diagnostic criteria drawn from the cited sources and is not based on new observations; the recurrence figures for LPC and BOC are those reported in the reference systematic review¹².

Feature	LPC	BOC	OKC	GOC
Epithelial lining	Thin non-keratinised squamous or cuboidal, 1-5 cell layers	As LPC, but within multiple cystic compartments separated by fibrous septa	Uniform parakeratinised squamous, 5-8 cell layers, corrugated luminal surface	Non-keratinised squamous with a cuboidal or columnar surface layer
Basal layer	Flat, not palisaded	Flat, not palisaded	Palisaded and hyperchromatic	Not palisaded
Characteristic features	Focal nodular ("whorled") epithelial plaques containing glycogen-rich clear cells	The same plaques in a multicystic, grape-like architecture	Flat epithelial-connective tissue interface; luminal keratin; satellite (daughter) cysts may be present in the wall	Hobnail surface cells, intraepithelial microcysts and duct-like spaces, mucous cells, epithelial spheres, occasional cilia
Typical radiographic pattern	Unilocular, well corticated, interradicular	Frequently multilocular, outline may be scalloped	Uni- or multilocular; antero-posterior growth with limited expansion	Uni- or multilocular; often scalloped, with cortical expansion
Pulp vitality of adjacent teeth	Retained	Retained	Usually retained	Usually retained
Reported recurrence	Low (approximately)	Higher (approximately)	High	High

	tely 2.4%)	21.7%)		
Principal sources	[5,8,11]	[9,10,20]	[3,21]	[22]

Treatment Modalities and Reported Recurrence

The therapeutic options considered in this review are surgical enucleation, enucleation with peripheral curettage, marginal resection or peripheral ostectomy, marsupialisation or decompression, regenerative procedures (GBR and guided tissue regeneration, GTR), and — in the context of differential diagnosis rather than as a treatment for LPC — endodontic and endodontic-surgical procedures. Indications and operative sequences were reviewed against the WHO classification of odontogenic lesions¹¹ and the reference systematic review^{1,12}, supplemented by contemporary clinical studies and case reports identified in the narrative update. A schematic representation of the enucleation and GBR sequence is shown in Figure 2.

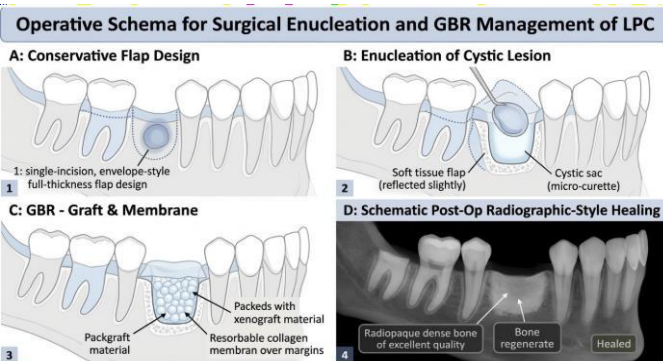


Figure 2. Schematic representation of the surgical sequence for enucleation of a lateral periodontal cyst with guided bone regeneration. (a) Conservative full-thickness envelope flap design. (b) Enucleation of the cystic lesion. (c) Placement of xenogeneic graft material with a resorbable collagen membrane over the defect margins. (d) Schematic representation of the expected appearance after bone healing. All four panels are diagrammatic illustrations prepared by the authors; panel

(d) is a schematic representation and not a radiograph of a patient.

Enucleation consists of the complete removal of the cystic sac by detachment from the surrounding bone walls. In the reference systematic review, enucleation was the most frequently described surgical approach for LPC, accounting for approximately 76% of cases in which a technique was specified, and the reported recurrence among cases with available follow-up was approximately 2.4%^{12,25,26,27}. The standard sequence comprises elevation of a full-thickness mucoperiosteal flap, conservative access osteotomy, complete removal of the cystic capsule, and routine submission of the specimen for histopathological examination — a step

that remains essential because of the documented discrepancy between clinical-radiographic and definitive histopathological diagnosis^{1,2,3,5,14,15,17}.

Peripheral curettage of the bone walls following enucleation is intended to eliminate residual epithelial remnants. It is reported more frequently for the botryoid variant, which is typically multilocular and larger than conventional LPC^{9,10,12,20,28}. In the reference systematic review, recurrence of approximately 21.7% was reported for BOC¹². These aggregated published data support the previously reported higher recurrence frequency of BOC compared with conventional LPC; they do not, however, constitute direct evidence of a distinct biological mechanism, and the caveats set out in Section 4.3 apply.

Peripheral ostectomy involves removal of a thin layer of bone surrounding the lesion after enucleation, again with the aim of eliminating epithelial remnants. The rationale has been extrapolated from the management of OKC, in which peripheral bone removal contributes to reducing recurrence^{21,24}. No prospective evidence supports its routine use in LPC or BOC. It should therefore be reserved for selected situations, such as recurrent lesions, extensive multilocular defects, or cases in which complete removal of the capsule cannot be confidently achieved intraoperatively^{10,12,24,28}.

Marsupialisation involves surgical opening of the cystic cavity and suturing of the lining to the oral mucosa, allowing progressive decompression and volume reduction. It is only exceptionally reported in LPC and occasionally described in BOC^{9,10,12}. Decompression is generally reserved for large odontogenic cysts, in order to limit surgical morbidity and preserve adjacent anatomical structures²⁴. Given the usually limited size and indolent behaviour of LPC, marsupialisation cannot be regarded as a standard therapeutic option, although it may be considered for selected large lesions or medically compromised patients^{10,12,24}.

Endodontic therapy is not a treatment for LPC but may be indicated when the differential diagnosis includes an inflammatory endodontic lesion, particularly a lateral radicular cyst or an apical granuloma associated with a non-vital tooth^{23,24}. Several publications have documented discrepancies between the initial clinical-radiographic diagnosis and the final histopathological diagnosis, with lesions initially interpreted as LPC subsequently confirmed as OKC or as other odontogenic cysts^{15,16,17,19,29}. Pulp vitality testing, radiographic re-evaluation after endodontic treatment, and surgical biopsy of persistent lesions therefore remain essential before a definitive diagnosis is established^{16,23,24}.

The distribution of surgical techniques reported in the reference systematic review is shown in Figure 6. For LPC, conservative enucleation predominated, with curettage and marginal resection reported less frequently. For BOC, the distribution was more heterogeneous, with enucleation and curettage reported in broadly similar proportions and marsupialisation only rarely¹². These proportions describe what has been reported in the published literature; they reflect historical practice and reporting habits and should not be read as an indication of comparative effectiveness.

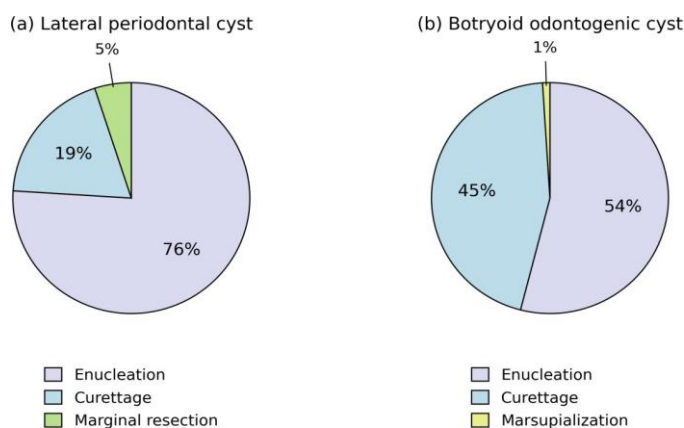


Figure 6. Distribution of surgical techniques reported for (a) lateral periodontal cyst and (b) botryoid odontogenic cyst. Percentages refer only to cases in which the surgical technique was specified and are reported as published in the systematic review of Chrcanovic and Gomez¹². The charts were redrawn by the authors from the published percentages; no re-analysis of the underlying data was performed. Values are rounded and may not sum to exactly 100%.

Regenerative Approaches

Regenerative adjuncts following cyst enucleation are documented almost exclusively in isolated case reports and small clinical series. They are generally proposed to avoid a persistent unfilled bone defect, particularly when periodontal support or alveolar ridge integrity may be compromised. The biological rationale of GBR rests on selective cell exclusion, clot stabilisation and space maintenance, which together favour osteogenic repopulation of the defect^{30,31}.

Within this low level of evidence, the following outcomes have been reported: radiographic bone fill within 6–12 months after enucleation combined with GTR^{13,32}; complete clinical and radiographic healing within 12–24 months after enucleation with xenogeneic or mixed grafts and resorbable collagen membranes^{33,34,35}; and satisfactory bone fill without recurrence after GBR in a maxillary LPC with buccal cortical expansion³⁴. A periodontal rationale has also been advanced, in which GBR is used where enucleation creates a defect that jeopardises the periodontal support of the adjacent teeth^{13,32}.

Reported regenerative strategies include guided tissue regeneration with bone grafts and barrier membranes, combined GBR approaches employing xenografts or allografts (including demineralized freeze-dried bone allograft, DFDBA), and platelet-derived biological adjuncts such as platelet-rich plasma (PRP) or platelet-rich fibrin (PRF)^{30,32,33,34,35}.

Overall, while regenerative adjuncts appear useful for the preservation of bone volume and periodontal support in selected defects, the available evidence is of low level and non-comparative. No controlled study has demonstrated a reduction in recurrence, or an acceleration of healing relative to spontaneous bone fill, after enucleation of LPC or BOC. Regenerative procedures should therefore be presented to patients as a means of managing the residual defect, not as a measure that reduces the risk of recurrence.

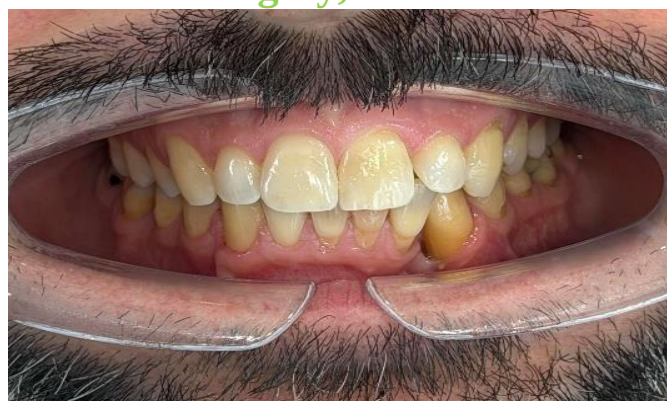
Illustrative Clinical Case

A 51-year-old healthy man presented with a slow-growing, painless swelling in the left mandibular incisor–canine region. The lesion had been present for several years and had progressively increased in size, prompting specialist evaluation. The medical history was non-contributory; the dental history included previous orthodontic treatment and regular professional oral hygiene care.

Intraoral examination showed a well-circumscribed, fluctuant swelling measuring approximately 9–12 mm at the mucogingival junction between teeth 32 and 33 (Figure 3). Both teeth responded normally to pulp vitality testing, and there were no signs of acute infection or periodontal involvement. Aspiration yielded clear fluid, consistent with a cystic lesion.



(a)



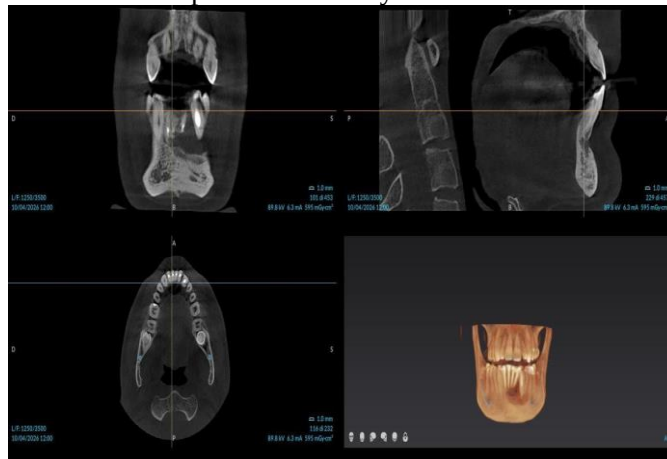
(b)



(c)

Figure 3. Illustrative case: preoperative clinical documentation. (a) Occlusal view of the mandibular arch showing the affected anterior sector. (b) Frontal intraoral view in maximum intercuspation. (c) Left lateral view showing the localised soft-tissue swelling at the mucogingival junction between teeth 32 and 33.

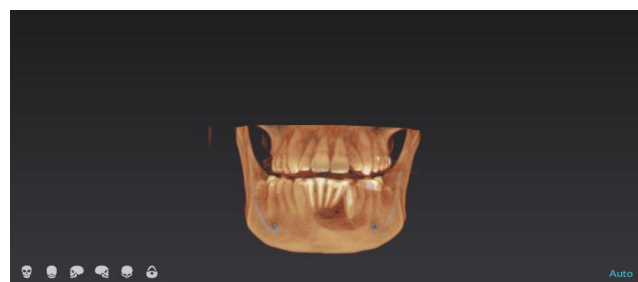
Radiographic assessment by panoramic radiography and CBCT demonstrated a well-defined interradicular radiolucency with a sclerotic margin, associated with mild root displacement but without loss of the lamina dura. CBCT confirmed thinning of both the buccal and the lingual cortical plates (Figure 4). On the basis of the clinical and radiographic findings, a provisional diagnosis of lateral periodontal cyst was established.



(a)



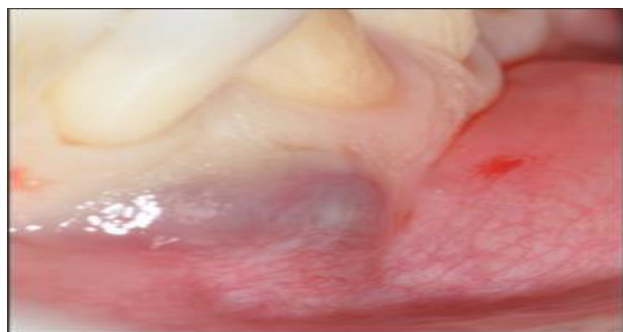
(b)



(c)

Figure 4. Illustrative case: preoperative cone-beam computed tomography. (a) Multiplanar reconstruction with three-dimensional rendering, showing a well-defined interradicular radiolucency with a corticated margin and thinning of both cortical plates. (b) Sequential cross-sectional slices through the lesion, illustrating its interradicular position and its relationship with the adjacent root surfaces. (c) Three-dimensional volume rendering of the mandible showing the extent of the osteolytic defect in the left anterior region.

Surgical treatment was carried out under local anaesthesia. A full-thickness mucoperiosteal flap was elevated, the lesion was enucleated in its entirety, and the bony cavity was curetted (Figure 5). The residual defect was reconstructed with a xenogeneic bone graft and a resorbable collagen membrane according to guided bone regeneration principles, and the flap was repositioned and sutured. The enucleated specimen was submitted in its entirety for histopathological examination.



(a)



(b)



(c)



(d)

Figure 5. Illustrative case: clinical and intraoperative sequence. (a) Preoperative vestibular view showing localised swelling of the periodontal tissues between teeth 32 and 33. (b) Intraoperative view after elevation of a full-thickness mucoperiosteal flap, showing the lesion in situ. (c) Intraoperative view after complete enucleation, showing the residual bony cavity. (d) Intraoperative view after flap repositioning and suturing.

Histopathological examination showed a thin, non-keratinised epithelial lining with focal epithelial plaques and clear cells, confirming the diagnosis of lateral

periodontal cyst. Photomicrographs of the specimen are not available and are therefore not presented; none of the figures in this article depicts histological material.

At the 12-month follow-up, the surgical site showed complete soft-tissue healing with radiographic evidence of progressive bone fill and no clinical or radiographic sign of recurrence. Teeth 32 and 33 continued to respond normally to pulp vitality testing. No intraoperative or postoperative complications were recorded.

DISCUSSION

The principal findings of this review can be summarised as follows. First, LPC and BOC are histologically related lesions that differ consistently, in the published aggregated data, in size, locularity and reported recurrence, with recurrence of approximately 2.4% for LPC and approximately 21.7% for BOC as reported in the reference systematic review¹². Second, the clinical and radiographic presentation of a lateral or interradicular radiolucency is insufficiently specific to exclude OKC, GOC or an inflammatory endodontic lesion, so that histopathological confirmation is indispensable^{3,15,16,17}. Third, conservative enucleation is the most frequently reported treatment for LPC and is associated with a low reported recurrence, whereas more extensive removal and longer surveillance are generally described for BOC¹². Fourth, regenerative adjuncts after enucleation are supported only by case-level descriptive evidence and have not been shown to influence recurrence. Fifth, the entire evidence base consists predominantly of case reports and retrospective series, which constrains the strength of every conclusion drawn below.

Clinical Implications

The most important practical implication is that clinical failure in this group of lesions arises more often from diagnostic error than from inadequate surgical technique. Pulp vitality testing and periodontal probing are the first discriminating steps, since endodontic-periodontal lesions occur only in the presence of pulp disease^{3,13,24}. CBCT provides a more accurate three-dimensional assessment of lesion boundaries, cortical involvement and the relationship with adjacent anatomical structures, and improves both diagnostic confidence and surgical planning; its use is reasonable for lesions larger than approximately 1 cm, for multilocular lesions and for lesions close to vital structures, in accordance with the principle of justified exposure^{23,36,37}. Histopathological examination of the entire specimen remains the reference standard^{1,2,3,5,14,16,29}.

Table 2 summarises a decision-oriented comparison of the principal surgical and conservative approaches, including the role of endodontic procedures in differential diagnosis. This comparison integrates the aggregated data of the reference systematic review¹², contemporary case-level clinical evidence identified in the narrative update, and the diagnostic principles of the WHO classification¹¹. It is an author-developed synthesis of published descriptive data and does not represent a graded recommendation; the "expected efficacy" column reflects what has been reported, not the result of comparative testing.

Table 2. Author-developed comparison of treatment modalities for lateral periodontal cyst and botryoid odontogenic cyst, including endodontic procedures in the context of differential diagnosis. Recurrence figures are those reported in the reference systematic review¹². No comparative trials exist; the table synthesises descriptive published data.

Approach	Main clinical indications	Reported outcome	Complications / limitations	Recurrence and follow-up	Cautions and "red flags"
Enucleation (± minimal curettage)	Typical LPC: vital tooth, unilocular, small to medium, well-circumscribed lesion	Most frequently reported approach for LPC; favourable bone healing described	Residual bone defect, interradicular dehiscence, transient sensitivity	LPC: low reported recurrence (~2.4%); radiographic review at 6 and 12 months, then individualised	Multilocularity, rapid growth or atypical size should prompt consideration of BOC, OKC or GOC
Enucleation with peripheral curettage	Thin-walled defects or suspected epithelial remnants; commonly reported in BOC	Reported for debulking of multilocular lesions	Larger surgical field; greater morbidity if aggressive	BOC: higher reported recurrence (~21.7%); prolonged follow-up	Proximity to vital structures (e.g. mandibular canal) requires caution and three-dimensional imaging
Marginal resection / peripheral osteotomy	Recurrent or extensive multilocular BOC; incomplete capsule removal	Rationale extrapolated from OKC protocols; not tested prospectively in LPC or BOC	Greater morbidity, bone loss, risk to adjacent teeth	Rarely reported for LPC; proposed for recurrent or extensive BOC	Not justified in typical LPC
GBR / GTR (bone graft ± membrane ± PRF/PRP)	Critical-sized defects jeopardising periodontal support (tunnel or through-and-through defects)	Case reports describe bone fill and periodontal recovery within 12–24 months	Technique-sensitive; risk of membrane exposure or infection; additional cost	Very low level of evidence; no controlled trials; no demonstrated	Poor plaque control, smoking, active infection or inability to achieve primary closure

Approach	Main clinical indications	Reported outcome	Complications / limitations	Recurrence and follow-up	Cautions and "red flags"
Marsupialisation / decompression	Rare in LPC; considered for large cysts or medically compromised patients	Gradual decompression and reduction in lesion size	Prolonged wound management; requires patient compliance	Exceptionally reported in LPC and BOC; prolonged surveillance advisable	Suspicion of an aggressive lesion should prompt biopsy and histological evaluation instead
Non-surgical endodontic therapy	Non-vital tooth or suspected inflammatory (lateral radicular) cyst	Effective for inflammatory endodontic pathology	Delayed diagnosis if the lesion persists	Persistence should prompt surgical biopsy	Never appropriate for LPC associated with a vital tooth; loss of vitality is the key discriminator
Endodontic surgery (apicoectomy, curettage, retrograde filling)	Persistent periapical pathology after root canal treatment	Appropriate only for lesions of endodontic origin	Surgical morbidity; apico-marginal defects	Not relevant to true LPC	Not indicated when the tooth is vital

On the basis of the reported recurrence patterns and of the published follow-up data, the following surveillance intervals appear reasonable, while acknowledging that no comparative study has validated any specific schedule: for LPC, radiographic review at 6 and 12 months followed by individualised long-term monitoring according to lesion size and surgical extent; for BOC, prolonged

surveillance of at least 5 years, given the higher reported recurrence and frequent multilocularity^{9,10,12,28}; for OKC, long-term monitoring of up to 10 years because of the possibility of late recurrence^{21,24}; and for GOC, follow-up of at least 5 years, with most reported recurrences occurring between the third and fifth year²².

Proposed Diagnostic and Therapeutic Algorithm

The algorithm presented in Figure 7 is an author-developed clinical synthesis based on the reviewed literature and the diagnostic principles outlined in the 2022 WHO Classification¹¹. It has not been externally validated and should therefore be considered a decision-support framework rather than a validated clinical pathway.

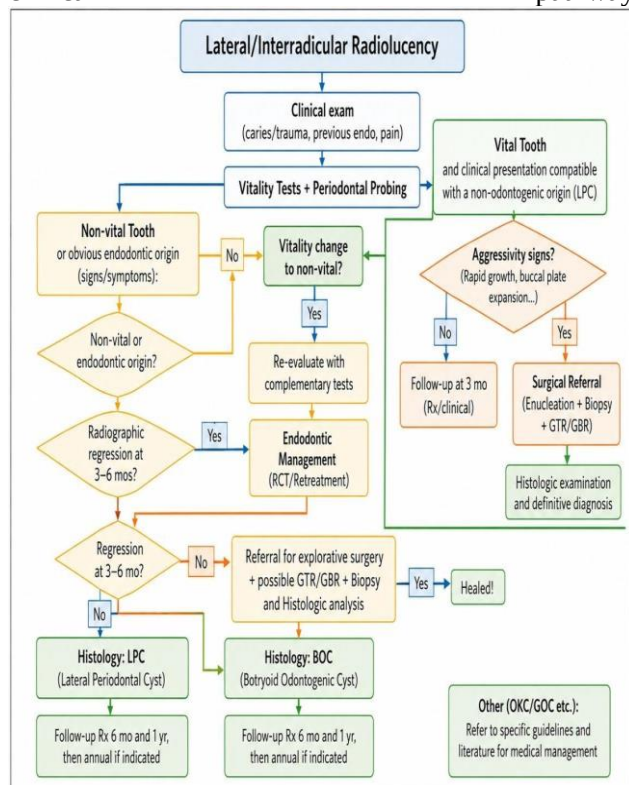


Figure 7. Proposed diagnostic and therapeutic framework for lateral and interradericular radiolucencies. The framework is an author-developed clinical synthesis based on the reviewed literature and on the diagnostic criteria of the 2022 WHO Classification¹¹. It has not been externally validated and is intended as decision support rather than as a validated clinical pathway.

The framework is organised around three sequential principles. Pulp vitality is the first decision point, because endodontic-periodontal lesions occur only in the presence of pulp disease; vitality and probing tests are therefore mandatory before any other consideration^{3,13,24}. Targeted imaging is the second: periapical radiography is adequate for small, well-circumscribed interradericular lesions, whereas CBCT is preferable when the lesion exceeds approximately 1

cm, appears multilocular, or lies close to vital structures^{23,36,37}. Histopathological examination is the third and decisive step, since the definitive diagnosis — and hence the follow-up plan — cannot be established on clinical and radiographic grounds alone, particularly in the presence of "red flag" features such as multilocularity, rapid expansion or cortical perforation^{1,2,3,5,14,16,29}.

The intended use of the framework is to reduce two opposite errors: undertreatment and inadequate surveillance of a lesion that proves to be OKC or GOC, and overtreatment of a small, indolent LPC. Its clinical value has not been measured, and it should be applied with clinical judgement rather than followed mechanically.

Limitations and Evidence Gaps

Several limitations constrain the conclusions of this review and the confidence that can be placed in the figures reported here.

- Level of evidence. The literature on LPC and BOC consists predominantly of case reports and retrospective case series. No randomised controlled trial and no prospective comparative study of treatment modalities exists for either lesion. Every therapeutic statement in this article therefore rests on descriptive evidence.
- Nature of the quantitative data. All aggregated figures reported here derive from a single previously published systematic review¹². The present authors performed no independent screening, extraction, appraisal or re-analysis, and no formal assessment of the methodological quality or risk of bias of the underlying publications was carried out for this article.
- Heterogeneity and incomplete reporting. The underlying publications differ widely in the completeness of their clinical, radiographic and histological documentation, and in follow-up duration. Denominators vary between variables, since percentages refer only to cases in which the variable was recorded, and the large standard deviations for BOC size and follow-up reflect this heterogeneity. Aggregated recurrence figures computed across series with markedly different surveillance periods are likely to underestimate true recurrence, particularly for lesions that may recur late.
- Publication and selection bias. Case reports preferentially describe unusual, instructive or successful cases, and recurrences may be under-reported. The reported recurrence figures should therefore be read as the frequency of recurrence reported in the published literature, not as an estimate of the true recurrence risk. The present

narrative update was restricted to publications in English and to three databases, so relevant work published in other languages or indexed elsewhere may have been missed.

- Absence of independent synthesis in the present article. Because no *de novo* systematic search, duplicate selection or quantitative synthesis was undertaken, this review inherits both the strengths and the limitations of its reference source and cannot correct for them. The targeted update was not systematic and is not reproducible in the sense required of a systematic review.
- External validation of the algorithm. The proposed framework has not been validated in any external cohort, has not been compared with usual care, and has not been evaluated for its effect on diagnostic accuracy, treatment selection or patient outcomes.
- The illustrative case. A single case cannot support inference about effectiveness. Histological photomicrographs are not available for this case, and the histopathological diagnosis is documented only by the descriptive report reproduced in Section 3.5.

Beyond these limitations, the following specific gaps in the evidence deserve attention. There is no prospective comparative trial of enucleation alone versus enucleation with GBR or GTR in terms of periodontal and bone outcomes^{12,30}. Outcome definitions are not standardised: clinical healing, radiographic healing and "absence of recurrence" are variously defined, and follow-up schedules are not uniform¹². The optimal management of BOC remains unclear, particularly the real benefit of adjuvant measures such as peripheral ostectomy^{9,10,12,28}. Diagnostic misidentification between LPC, OKC and GOC persists and has not been systematically quantified in contemporary practice^{5,16,23,29}. Finally, the regenerative materials discussed in Section 4.4 have not been evaluated in cyst-related alveolar defects.

Future Perspectives

Several regenerative technologies developed for other indications may in principle be relevant to the reconstruction of post-enucleation defects, but none has been evaluated in LPC or BOC, and all are reported here as directions for research rather than as clinical options.

Xenogeneic cortical bone laminae have been used as barrier systems in GBR, where their mechanical stability and natural collagen matrix allow graft

containment and space preservation; long-term follow-up of lamina-supported GBR has described stable bone volume and periodontal integrity beyond 36 months³⁸. Reconstruction of extensive alveolar and mucosal defects using a xenogeneic cortical sheet (Flex Cortical Sheet) has been described in a clinical case report³⁹. Both sources concern alveolar ridge reconstruction, not cyst-related defects; their applicability to interradicular or through-and-through defects following cyst enucleation is therefore an extrapolation and has not been validated for LPC or BOC.

A magnetic-dam barrier intended to improve graft sealing and reduce micromovement at the regenerative interface has been described in a laboratory study⁴⁰. This evidence is *in vitro* and preclinical; the device has not been evaluated in patients, and no clinical claim can be made for it in the management of cystic bone defects.

Pharmacological modulation of bone metabolism has also been proposed as a means of enhancing regeneration. *In vitro* work on MG-63 and MC3T3-E1 osteoblastic cell lines has shown that raloxifene, a selective oestrogen receptor modulator, influences osteoblastic proliferation and gene expression through an oestrogen receptor-mediated mechanism, with cell-type-dependent effects⁴¹. These findings derive entirely from cell culture and concern neither cystic bone healing nor any clinical indication; whether raloxifene-functionalised scaffolds have any translational value after cyst enucleation is unknown and untested. Similarly, an association between platelet count and the healing of post-extraction sites has been reported in a retrospective observational study⁴², but this relates to extraction sockets rather than to cystic defects.

The priorities for future research are therefore clear. Prospective comparative studies of enucleation with and without regenerative adjuncts, using standardised definitions of clinical and radiographic healing and predefined follow-up intervals, are needed before any regenerative protocol can be recommended for LPC or BOC. Registry-based collection of BOC cases with mandatory minimum follow-up would provide a more reliable estimate of recurrence than the aggregation of heterogeneous case reports. Finally, prospective evaluation of a diagnostic pathway such as the one proposed here measuring its effect on the rate of histologically confirmed misdiagnosis would establish whether structured decision support improves outcomes in practice.

CONCLUSION

Lateral periodontal cyst is a biologically low-risk but diagnostically demanding lesion. Conservative surgical enucleation is the most frequently reported management

and is associated with a low reported recurrence, but a satisfactory outcome depends primarily on accurate histopathological diagnosis, because the radiographic presentation of LPC may be reproduced by lesions with a substantially higher recurrence potential.

The aggregated published data support the previously reported higher recurrence frequency of the botryoid variant compared with conventional LPC and justify more careful margin control and more prolonged surveillance in multilocular, extensive or recurrent lesions. These figures derive from heterogeneous case-level literature and should be interpreted as descriptive rather than as validated risk estimates.

From current evidence, the following practice points can be outlined. Pulp vitality testing, periodontal assessment and appropriate imaging should always precede treatment, with CBCT reserved for large, expansile or multilocular lesions and for lesions adjacent to vital structures. The excised specimen should always be submitted in its entirety for histopathological examination, since clinical and radiographic evaluation alone carries a substantial risk of misdiagnosing OKC or another odontogenic cyst. Typical LPC should be treated by conservative enucleation with minimal curettage, followed by radiographic review at 6 and 12 months and individualised monitoring thereafter. Critical-sized bone defects may be managed with guided bone or tissue regeneration, on the understanding that this evidence is case-level and that no effect on recurrence has been demonstrated. BOC and multilocular presentations warrant careful margin control, consideration of adjuvant measures and prolonged follow-up. Endodontic and periapical surgery should be undertaken only when endodontic pathology is confirmed and are never primary treatments for LPC in a vital tooth.

The diagnostic and therapeutic framework proposed in this article is an author-developed clinical synthesis, not a validated pathway. Prospective comparative studies with standardised outcomes and adequate follow-up remain the principal unmet need in this field.

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Author Contributions

Conceptualisation, F.B., L.M., S.F., G.L.U. and G.L.; methodology, S.S., L.M. and D.A.; investigation, S.F., G.L.U. and G.L.; data curation, S.F., G.L.U. and G.L.; formal analysis, S.F., G.L.U., G.L. and L.M.; writing — original draft preparation, S.F., G.L.U. and G.L.; writing — review and editing, L.M., S.S. and D.A.; supervision, L.M.; project administration, L.M., S.S. and D.A. All authors have read and agreed to the submitted version of the manuscript.

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Competing and Conflicting Interests

The authors declare that they have no competing or conflicting interests.

Ethical Approval

This article reports a narrative review of published literature together with one illustrative clinical case. The case was managed as part of routine clinical care, and all procedures involving the patient were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. No Ethics Committee approval is required in Italy for studies carried out in private settings.

Informed Consent

Written informed consent for publication of the clinical data and images relating to the illustrative case was obtained from the patient. The signed consent form is retained and archived by the authors and is available to the editorial office on request.

Data Availability

All data discussed in this review are contained within the cited published sources. No new dataset was generated or analysed for this article.

Abbreviations

The following abbreviations are used in this manuscript:

BOC	Botryoid odontogenic cyst
CBCT	Cone-beam computed tomography

DFDBA	Demineralised freeze-dried bone allograft
FDI	Fédération Dentaire Internationale (two-digit tooth notation)
GBR	Guided bone regeneration
GCA	Gingival cyst of the adult
GOC	Glandular odontogenic cyst
GTR	Guided tissue regeneration
LPC	Lateral periodontal cyst
OKC	Odontogenic keratocyst
PRF	Platelet-rich fibrin
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRP	Platelet-rich plasma
SI	Système International (International System of Units)
WHO	World Health Organization

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