Analysis of Marsupialization of Mandibular Cysts in Improving the Healing of Related Bone Defects

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Purpose: Marsupialization, designed to reduce the mandibular cyst volume, has continued to debated regarding its influence on the healing of the related bone cavity. The aim of the present study was to evaluate the 3-dimensional radiographic variation over time in mandibular odontogenic cystic lesions after marsupialization and assess the correlations between these variations and variables that can affect the procedure.

Materials and Methods: We planned a retrospective cohort study. The predictor variables were the treatment duration, preoperative volume, patient age, histologic type, and number of preoperative residual bony walls. The outcomes variables were the postoperative volume reduction and the daily reduction rate calculated using computed tomography (CT) from before to after marsupialization using software designed for volumetric reconstruction and measurement of cyst-related bone defects. The descriptive and bivariate statistics were computerized, and the significance level was set at $P = .05$.

Results: The sample included 15 patients (12 men and 3 women; mean age, 51.6; range, 27 to 85 years) affected by keratocysts (n = 6), dentigerous cysts (n = 6), and radicular cysts (n = 3) who had undergone marsupialization. The median duration of marsupialization was 406 days (25th to 75th percentile, 276 to 519). The mean ± standard deviation (SD) pre- and postdecompression volumes were 6,908.27 ± 2,669.058 and 2,468.13 ± 1,343.517 mm^3, respectively ($P < 0.001$), and the mean ± SD percentage of reduction was 63.90 ± 13.12%. The volume decrease in the bone defects correlated positively with the treatment duration ($P = .009$) and preoperative volume ($P < .001$). However, no correlation was found with the other variables ($P > .05$) nor between the daily reduction rate and other variables ($P > .05$).

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Conclusions: Marsupialization appears useful in improving the healing of cyst-related bone defects in mandibles, especially larger defects. Further studies with a wider sample size would add more knowledge to this topic.

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The so-called conservative treatment of voluminous cystic lesions of the jaw (ie, cystostomy) aims to release the intraluminal pressure, allowing a gradual growth of the surrounding bone with progressive volume reduction before performing lower risk enucleation.[1-5] Two methods have been reported, each with advantages and disadvantages. Marsupialization, as described by Partsch,[3,4] transforms the cystic intrabony defect into an accessory pouch of the oral cavity through wide exposition of the inner compartment of the lesion. This involves ostectomy of the occlusal and vestibular cortical bone, partial removal of the external cystic wall, and suturing of the mucosal flap to the cystic intrabony defect or the bone outline. This procedure generally requires frequent gauze packing or the application of obturators to prevent food impaction and infection.[3,6-8] Apart from the release of inner pressure, the healing process with volume reduction of the lesion benefits from the creeping invasion of the oral mucosa on the cystic lining. Decompression, as proposed by Neuschmidt[9] and Thoma,[10] creates a minimal epithelial pathway through the soft tissues between the intrabony compartment and the oral environment after the mucosal flap has healed around a drainage tube or stent. This is maintained in situ until the epithelial lining of the wound edge is complete. Decompression appears to be better tolerated than marsupialization[11,12]; however, this depends on patient compliance with daily rinsing using a blunt needle through the epithelial slit to maintain patency.[8,12,13]

Previous studies that used these 2 techniques have been limited, in particular, because the 2 techniques have no precise distinctions between them and they have often been used in the same trials and for approximate radiologic bidimensional evaluation of lesion shrinkage over time.[14-17] Computerized volumetric measurements of cyst reduction using computed tomography (CT) scans are known to correlate with important variables after decompression.[12,13,18-20] Also, the same method of evaluation has been used to investigate the marsupialization of 15 keratocysts[21] and 2 cases of dentigerous cysts.[22] Increased understanding of marsupialization could determine the effective duration of treatment before performing definitive low-risk enucleation of the lesion and the variables that can affect the outcomes, which could establish the timing of the radiologic evaluations. This approach would allow us to compare marsupialization and decompression, which has been better documented in reported studies, and verify whether a difference exists in the outcomes, allowing us to choose the more appropriate technique for specific clinical situations.

The purpose of the present study was to investigate the marsupialization procedure in terms of the radiologic volumetric reduction of different types of mandibular cyst-related defects. We hypothesized that the timing of bone healing could be correlated with some therapeutic, anatomic, histologic, and demographic variables. The specific aims of the present study were to estimate the relevance of these variables in improving the healing of the hard tissues of the lower jaw.

Materials and Methods

STUDY DESIGN AND SAMPLE

To address the research purpose, we designed and implemented a retrospective cohort study. The study population included all patients who had undergone marsupialization of mandibular cystic lesions from January 1, 2013 to December 31, 2013 at the Dentistry and Oral–Maxillofacial Surgery Unit, University of Modena and Reggio Emilia (Modena, Italy) and had met the inclusion criteria.

The inclusion criteria were as follows: age 18 to 85 years; a mandibular lesion clinically and histologically defined as a cyst; cyst dimensions and closeness to important anatomic structures requiring conservative Partsch I treatment and delay of enucleation to at least 6 months later; and the availability of 2 cone-beam CT (CBCT) radiologic examinations before and a few weeks after surgical marsupialization. The exclusion criteria were as follows: age less than 18 years or greater than 85 years; patient failure to return for follow-up; and patient inability to provide written informed consent for authorization of the collection and analysis of nonsensitive data. Our local ethics committee, "Comitato Etico dell'Area Vasta Emilia Nord," approved the present study (approval no. AOU 0005163/19); all participants provided written informed consent.

The CBCT scans were performed at different intervals for each patient. When 2 or more postoperative CBCT scans were obtained, the last scan before the enucleation procedure was used to perform the volume reduction calculations. The second CBCT was performed to obtain sufficient details regarding the status of the healing process to establish the timing of cyst enucleation, with particular attention to new bone formation on the vestibular and lingual sides of the mandible, the alveolar canal position with respect to the lesion, and involvement of the teeth. Descriptive data are summarized in Table 1.

All marsupialization procedures were performed with the patient under local anesthesia. Marsupialization included mobilization of a vestibular full-thickness trapezoidal flap, exposure of the cyst lining after ostectomy of the buccal bone plate, partial removal of the external cystic wall with a scalpel, and closure by suturing the edges of the remaining lesion with the flap borders or anchoring them to the vestibular bone outline. The cyst wall specimens were sent for histologic analysis. Gauze soaked with an antibiotic agent was applied to the newly formed accessory pouch. After surgery, oral antibiotic therapy (amoxicillin, 3 g/day for 7 days) and a nonsteroidal analgesic drug (ibuprofen, 600 mg/day) were prescribed. The patients were instructed to adhere to a soft diet for 1 week and to maintain appropriate oral hygiene, with twice daily rinsing using 0.2% chlorhexidine mouthwash. The gauze and suture were removed 7 days after surgery, and new gauze was inserted into the surgical pouch after disinfection with 0.2% chlorhexidine. The patients were monitored clinically with visits every week until the definitive operation time. The visits included cleaning of the cavity and application of new gauze soaked with an antibiotic agent. The clinical and radiologic images of 1 patient are shown in Figures 1 to 5.

CBCT was performed in all cases using a NewTom VGi scanner (Quantitative Radiology, Verona, Italy). This apparatus was set for an exposure time of 15 seconds at 110 kV and 8 mA. The imaging area (field of view) was a cylinder with a height of 80 mm, diameter of 120 mm, and pixel size of 100 μm. Contiguous cross-sectional images with a slice width of 0.5 mm in 3 directions (ie, parallel to the dental arch, perpendicular to the dental arch, and horizontal) were reconstructed from the projection data. Data from the preoperative CBCT scans and those from the last CBCT scan before the enucleation procedure for each patient were saved in Digital Imaging and Communication in Medicine file format and transferred to a workstation (Mac Pro Air Quad; 2.66 GHz; Apple Corp, Cupertino, CA) to be visualized and analyzed using Amira imaging software, version 5.3.3 (Visage Imaging GmbH, Berlin, Germany). The grayscale density between the chromatic representation of totally or partially mineralized bone and the lesion was set by an expert radiologist for each examination. Segmentation was performed manually using the dedicated editing tool to select the cystic area in each slide in the 3 spatial projections (ie, coronal, axial, and sagittal) concurrently with the 3-dimensional (3D) visual examination. The areas were rendered together using the tool "material statics—total volume" to obtain the volume measurements. For each patient, a preoperative (initial) volume (Vi) and a postoperative (final) volume (Vf) were calculated from the appropriate CBCT scans. The segmentation procedure for a cystic lesion using the Amira software for digital mandibular 3D model reconstruction and volumetric measurements is shown in Figures 6 to 9.

Table 1. DESCRIPTIVE SUMMARY OF STUDY SAMPLE

Study Variable	Descriptive Statistics
Sample size (n; %)	15 (100)
Male gender (n; %)	12 (80)
Age (yr)	
Median	50
Range	27-85
Histologic type (n; %)	
Keratocyst	6 (40)
Dentigerous	6 (40)
Radicular cyst	3 (20)
Walls (n; %)	
4	3 (20)
5	8 (53.3)
6	4 (26.7)

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STUDY VARIABLES

The following variables, quite heterogeneous, were considered as predictor variable: *1)* treatment duration, *2)* preoperative volume, *3)* patient age, *4)* histologic type, and *5)* number of preoperative residual bone walls. The primary outcome variables were the total and percentage of cyst volume reduction, calculated as (Vi − Vf) and [(Vi − Vf)/Vi] × 100, respectively. The secondary outcome variables were the daily reduction rate, calculated using the formula (Vi − Vf)/time (in days), and the daily percentage of reduction, calculated using the formula $[1 - (Vi - Vf^1)/\text{time (in days)}] \times 100$, for each patient.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS (IBM Corp, Armonk, NY). A *t* test for paired data was used to compare the volume at baseline and after treatment. The normality of the data distributions was assessed using the Shapiro-Wilk test. After a bivariate analysis (Pearson's correlation), a linear model was used to estimate the association between the dependent and independent variables. The significance level was set at $P = .05$.

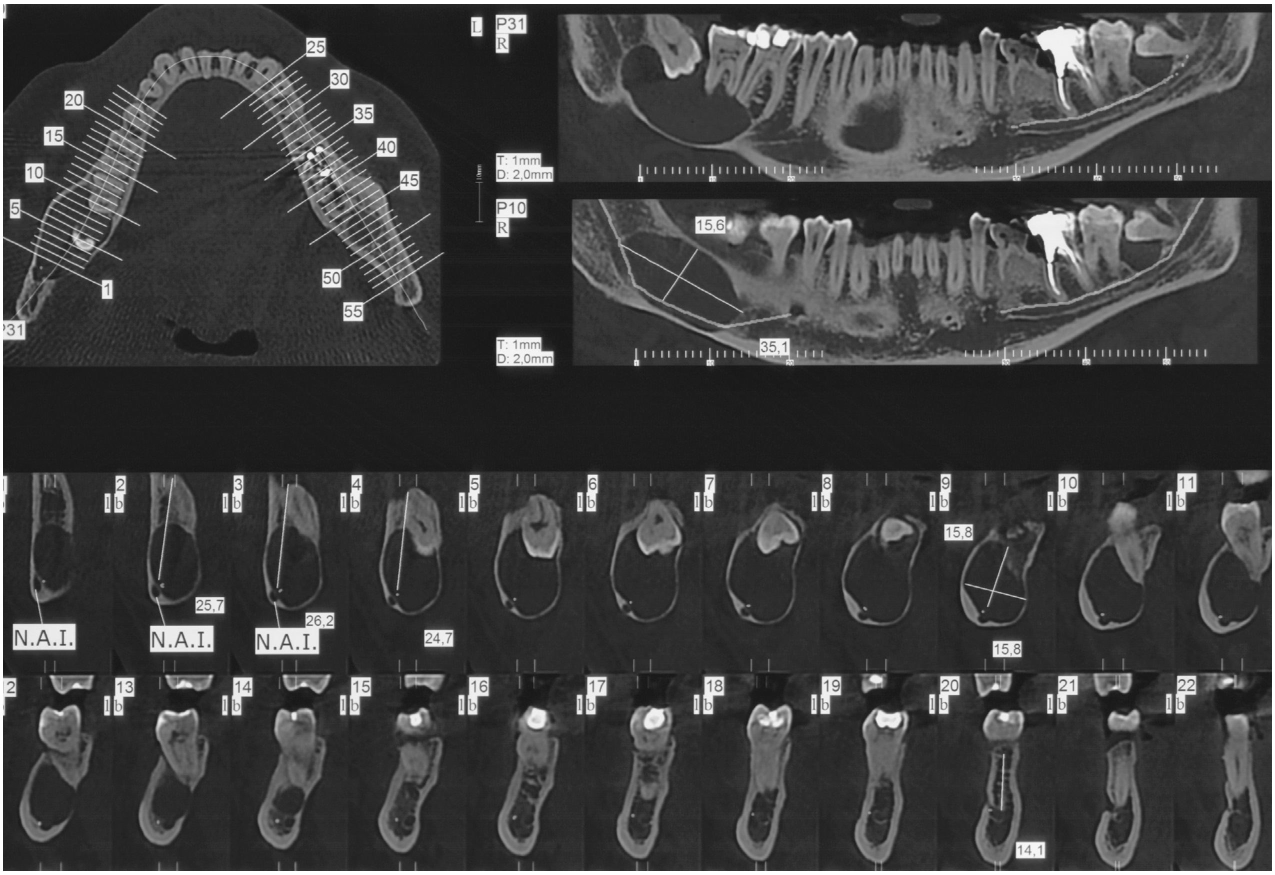

FIGURE 1. Cone-beam computed tomography cross-sectional slices before marsupialization showing a dentigerous cyst in the right mandible.

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Results

The present study included 15 subjects (12 men and 3 women), with a mean age of 51.6 years (range, 27 to 85) and a total of 15 mandibular lesions. The lesions consisted of keratocysts in 6, dentigerous cysts in 6, and radicular cysts in 3. The postoperative period before enucleation was uneventful for all 15 patients. The mean duration of marsupialization was 408.2 days (13.6 months; range, 194 [6.5 months] to 689 days [20.2 months]). The mean ± standard deviation (SD) pre- and postmarsupialization volumes were 6,908.27 ± 2,669.058 and 2,468.13 ± 1,343.517 mm^3, respectively, a statistically significant difference (t = 8.44; df = 14; P < .001; 95% confidence interval, 3,313.052 to 5,567.215). The mean absolute and mean percentage of volume reduction were 4,440.1 ± 2,035.2 mm^3 and 63.9 ± 13.12%, respectively. The mean ± SD amount of daily reduction (DR) and the percentage of reduction were 11.3 ± 5.27 mm^3 and 0.17 ± 0.06%, respectively. The linear regression model (adjusted R^2, 0.78) showed a significant positive association between the volume reduction and treatment duration (P = .009) and preoperative volume (P < .001) but not with age (P = .789). No correlations were found between the DR amount and the treatment duration (P = .383) or the preoperative volume (P = .68). However, a correlation was found between the DR amount and the preoperative volume for dentigerous cysts only (P = .04). Pearson's correlation coefficients for the continuous variables and bivariate analysis results for the categorical variables, with volume reduction as the primary outcome, are reported in Table 2.

No significant difference was found in the amount of volume reduction among the histologic types (F = 0.304; df = 3; P = .822) or among the cysts with different numbers of preoperative residual bone walls (F = 0.799; df = 2; P = .5). Also, no significant difference was found in the amount of DR among the histologic types (F = 1.942; df = 3; P = .241) or according to the number of preoperative residual bone walls (F = 3.550; df = 2; P = .11). A scatterplot of the relationship between the volume reduction and duration of treatment and preoperative volume is shown in Figure 10.

The regression model of the predictor variables versus the primary outcome variable is presented in Table 3. The predictor variables associated with the

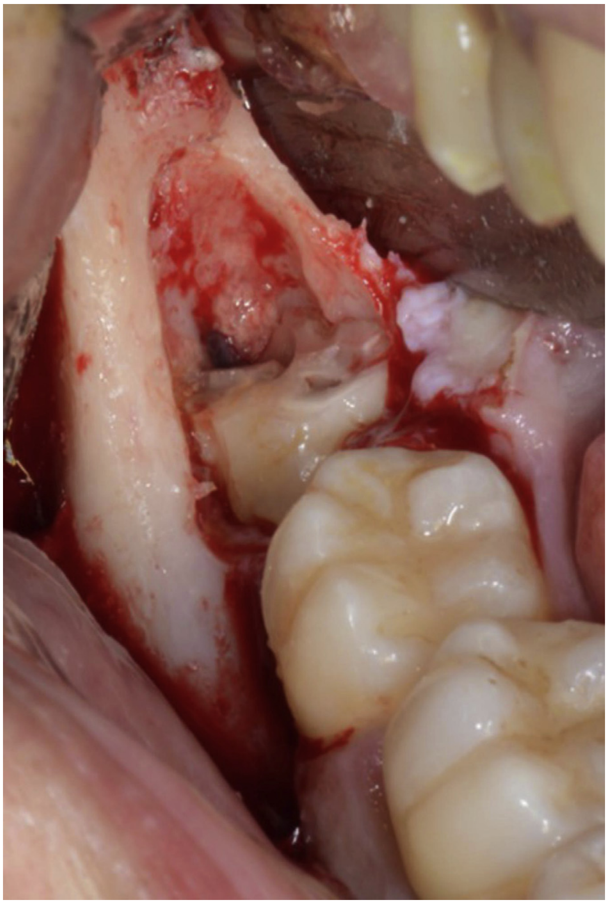

FIGURE 2. Intraoperative photographs showing tooth removal during marsupialization of the same lesion shown Figure 1.

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FIGURE 3. Intraoperative photographs showing opening of the cyst during marsupialization of the same lesion shown in Figure 1.

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primary outcome variable after adjustment for potential confounders were the preoperative volume and treatment duration.

Discussion

The purpose of the present study was to investigate the marsupialization procedure in terms of the radiologic volumetric reduction for different types of mandibular cyst-related defects. We had hypothesized that the entity and timing of bone healing would correlate with some therapeutic, anatomic, histologic, and demographic variables. The specific aims of the present study were to estimate the relevance of these variables in improving the healing of the hard tissues of the lower jaw.

Through this project, we sought to add to the knowledge of marsupialization via the proper evaluation of the radiographic modifications of the related bone cavities. We hypothesized that some factors would be relevant to improving the final result. Specifically, the aim of the present study was to achieve a better understanding of the indications and the usefulness of such a straightforward approach. The correlations between the outcome variables, bone defect reduction, and the daily rate of reduction, obtained using a highly reliable method and including 6 important variables (3 quantitative and 3 qualitative), support the conclusion that a longer treatment duration and larger lesions were associated with more successful intervention in terms of cyst cavity shrinkage. The daily reduction rate correlated with the initial volume only for dentigerous cysts, in agreement with the findings reported by Lizio et al.[12] The lack of significant associations with the other variables supports the usefulness of cystostomy in every critical case of cystic lesions of the lower jaw.

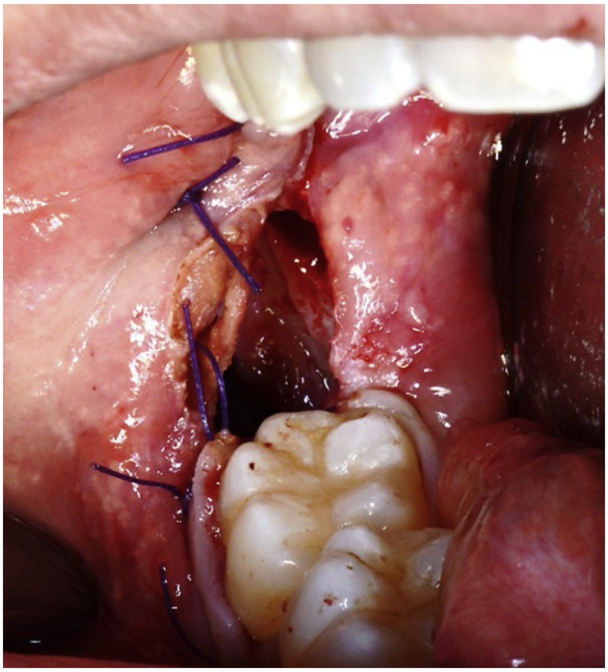

FIGURE 4. Intraoperative photographs showing opening of the cyst during marsupialization of the same lesion shown in Figure 1.

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Our results agree with previous reports on decompression that used 3D computerized evaluations. This minimally invasive procedure resulted in volume reduction of 48.28 to 57.95% for various types of cysts after ~6 months (monthly mean rate, 11.4%) and a reduction of 70.5% after 8 months (monthly reduction rate, 8.81%) in residual bone cavities after dentigerous cyst removal.[8] Apart from Song et al,[19] who showed an association with age, no variables were found to be associated with the extent of volume reduction after decompression, excluding the treatment duration and the initial volume. Because the 2 techniques (ie, marsupialization and decompression) showed similar results in terms of cystic cavity shrinkage, the size of the communication between the cyst compartment and the oral cavity might be irrelevant. Shudou et al[21] reported no differences in the treatment results when stratified by the window size, and Song et al[19] observed that the number of drains was not associated with the rate of volume reduction. It is possible that, regardless of the size of the aperture, the positive pressure gradient disappears during cystostomy, and the persistence of a similar pressure inside and outside the intraosseous defect in communication with the oral cavity will guarantee a reduction in the bone

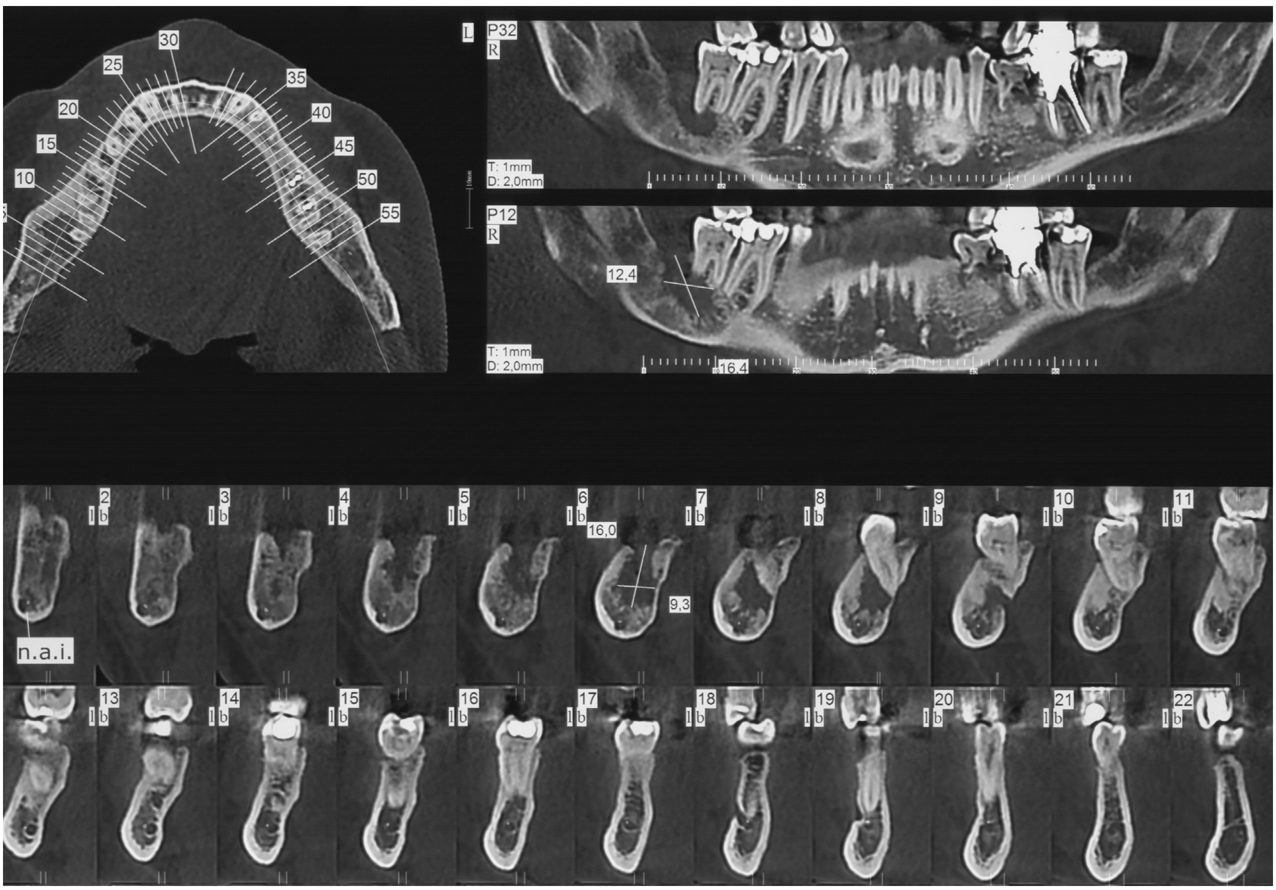

FIGURE 5. Cone-beam computed tomography cross-sectional slices after marsupialization and just before enucleation of the same lesion shown in Figure 1.

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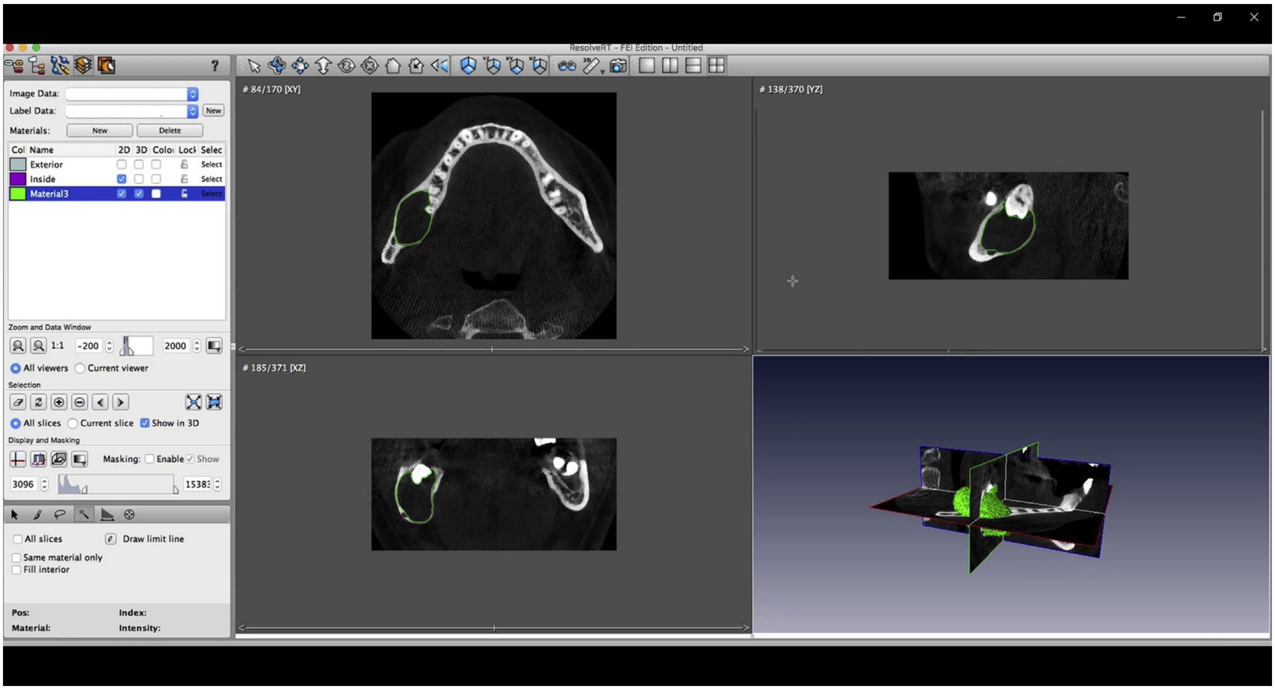

FIGURE 6. Cone-beam computed tomography scan showing segmentation procedure and volumetric measurements of the dentigerous cyst before marsupialization. The lesion profile is outlined on each slice in 3 spatial planes, providing a 3-dimensional rendering of the affected portion.

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cavity over time. Hence, the positive pressure gradient inside the cystic compartment could be the most important factor causing cyst development. The creation of a bone cavity partially lined by the cystic wall after marsupialization or decompression reduces the physical and biomolecular mechanisms responsible for cyst enlargement, which are connected and have been only partially characterized.

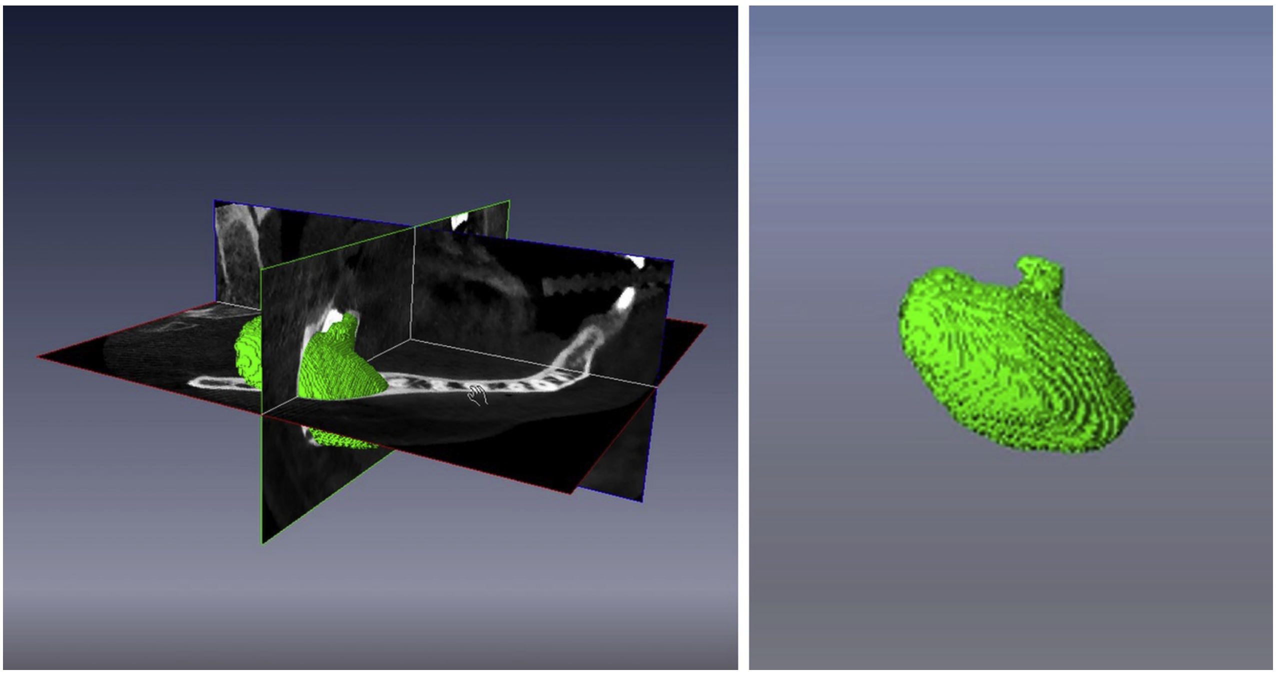

FIGURE 7. Graphic representation of the cystic volume before marsupialization with and without the treatment plan.

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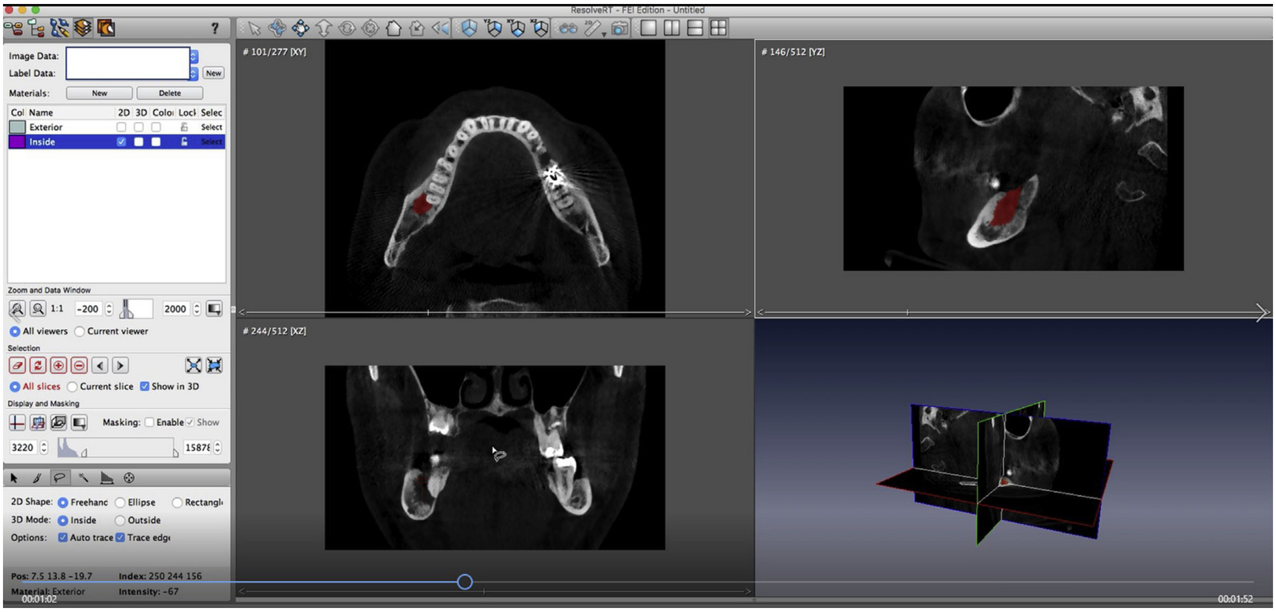

FIGURE 8. Cone-beam computed tomography scan showing segmentation procedure and volumetric measurements of the dentigerous cyst at the end of marsupialization. As in the preoperative evaluation, the lesion profile was outlined on each slice in 3 spatial planes, providing a 3-dimensional rendering of the affected portion.

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The conservative approach eliminates the surrounding bone surface tension, which inhibits the proliferation and differentiation of osteogenic precursors, induces signaling pathways to promote osteogenesis, and modulates the expression of osteonectin and collagen type I. Sun et al[23] analyzed the osteogenic differentiation of orofacial bone marrow stromal cells before and after marsupialization in odontogenic cysts. They concluded that cystostomy might play a role in the modulation of proliferation, stemness, and differentiation of the bone marrow stem cells by regulating the concentration of kinases.[23] Ninomiya et al[24] demonstrated that marsupialization or decompression significantly decreased the expression of interleukin-1α, playing an important role in bone resorption. Mechanical stimulation is known to promote the differentiation

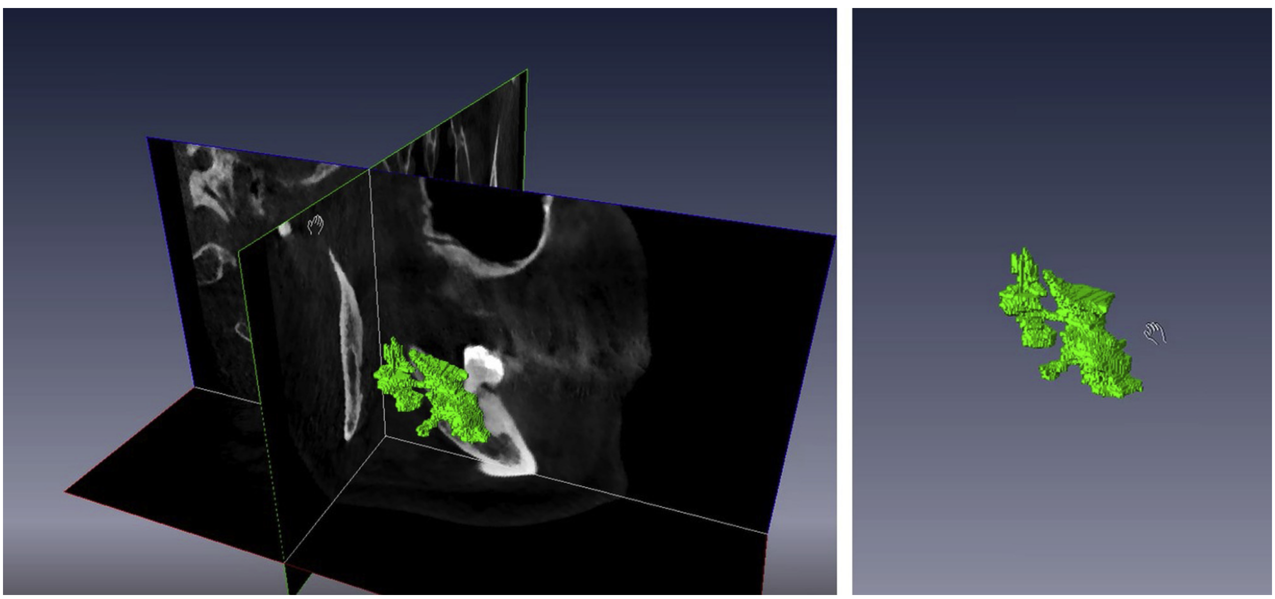

FIGURE 9. Graphic representation of the cystic volume after marsupialization with and without the treatment plan.

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Table 2. CORRELATION COEFFICIENTS BETWEEN PRIMARY OUTCOME VARIABLE (VOLUME REDUCTION) AND CONTINUOUS VARIABLES AND BIVARIATE ANALYSIS OF VOLUME REDUCTION AND CATEGORICAL VARIABLES

Variable	Volume Reduction	*P* Value
Correlation coefficient		
Time (days)	0.74	.002
Preoperative volume	0.87	<.001
Age	−0.72	.1
Mean ± SD		
Histologic type		.822
Keratocyst	4,615.83 ± 2,078.868	
Dentigerous cyst	4,156 ± 2,480.617	
Radicular cyst	5,475.5 ± 886.005	
Walls		.5
4	6,002 ± 791.751	
5	4,113.25 ± 1,201.545	
6	3,922.5 ± 3,530.182	

Abbreviation: SD, standard deviation.

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of human bone marrow stromal cells and osteoblast activities,[24,25] and previous studies in animal models observed that intermittent negative pressure promoted angiogenesis and osteoblastic differentiation of bone marrow stem cells with a faster healing time.[26-28] Recently, Castro-Nunez[29] applied a closed vacuum-like drain system connected to the internal cyst compartment to create a negative pressure gradient and stimulate bone formation. Castro-Nunez[29] reported that 1 large osseous defect affecting the mandibular symphysis had been filled with new bone within less than 2 weeks and that another osteolytic lesion had been reduced by more than 50% of the initial volume after only 11 days. However, the cystic wall has been shown to produce biochemical mediators such as collagenases, prostaglandins, and interleukins, which stimulate osteoclastogenesis and bone matrix destruction, which might be powered by internal pressure.[30-33] Without focusing on the complex biomolecular mechanisms, and independent of a communication between the intra- and extrabone compartments, the osteogenic process correlated positively with exposure of the bone cavity walls to the oral environment or to an external sucking action.

Chiapasco et al[34] reported residual bone cavity dimension reductions of 12.34, 43.46, and 81.30% at 6, 12, and 24 months, respectively, after cyst enucleation. Ihan Hren and Miljavec[35] reported mean increases in bone density of 7, 27, and 46% at 2, 6, and 12 months, respectively, after cystectomy. Both of these studies performed analyses using dedicated software orthopantomograms. These values are significantly lower than those reported in a previous study using 2-dimensional radiographic examinations, which reported 22.42, 46.07, and 64.69% increases at 1, 3, and 6 months after marsupialization, respectively,[14] and the previously cited results after decompression calculated from CT scans.[8]

Complete closure of the soft tissues isolating the residual bone defect from the oral cavity seems to slow the osteogenic process. This supports the use of the conservative treatment option, despite the objective disadvantages related to disinfection of the newly created cavity or maintenance of the patency of the

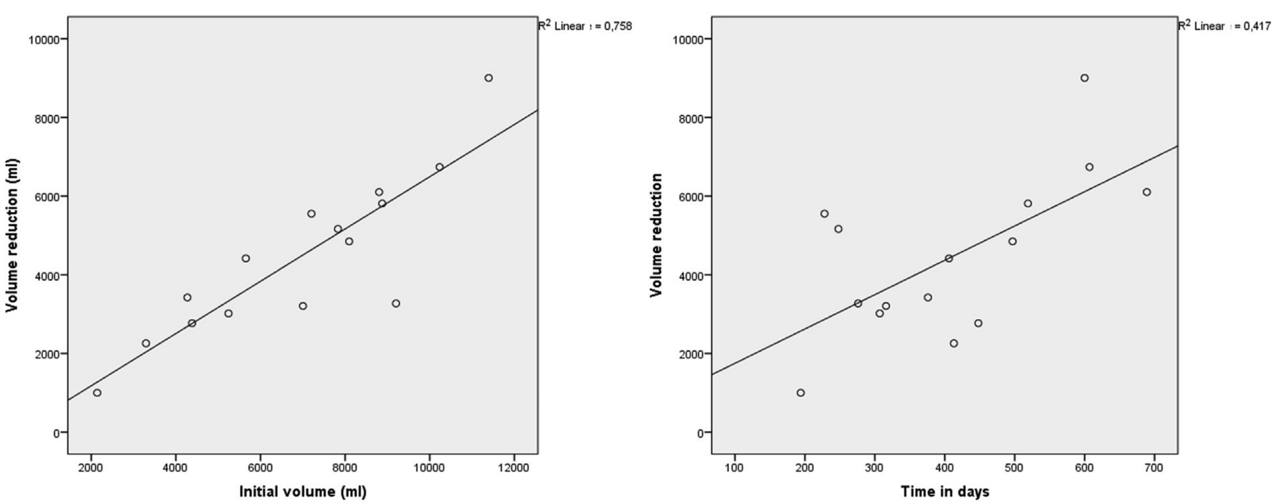

FIGURE 10. Q-plots of the duration in days and initial volume (in milliliters) compared with the cystic volume reduction after marsupialization. The linear regression line is shown.

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Table 3. REGRESSION MODEL OF PREDICTOR VARIABLES VERSUS PRIMARY OUTCOME VARIABLE

Variable	Coefficient for Volume Reduction	*P* Value
Time (days)	0.646	.009
Preoperative volume	0.871	<.001
Age	−0.76	.39
Histologic type	0.304	.822
Walls	0.799	.5

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communication slit during marsupialization and decompression, respectively. These procedures showed similar rates of cyst formation reduction and prevention of pressure gradient regeneration between the bone defect and oral environment, both fundamental to preventing epithelial remnant reorganization in a new lesion and supporting the osteogenic processes. Setting aside the question of patient discomfort, marsupialization guarantees the aperture of the bone defect. In contrast, decompression is prone to closure, with reintervention required in some cases.[8,12] However, marsupialization results in an apparently useless major loss of bone to create the pouch.

The duration of treatment and preoperative cystic volume both correlated positively with volume reduction, similar to decompression. Longer exposure of the bone cavity to the oral environment appeared to have a positive effect on bone healing. The reason this was more effective for larger cysts remains unclear. However, it might be associated with the connection of a major bone surface with the mouth, in contrast to the irrelevance of the number of bone defect walls. Nonetheless, the lack of significant associations with the other variables supports the usefulness of cystostomy in every critical case of cystic lesions of the lower jaw.

Marsupialization and decompression have been used to reduce the risk of damage to important anatomic structures associated with the invasive procedure of enucleation[8,12,36,37]; however, the low quality of the investigative methods used has limited the knowledge and use of conservative techniques in clinical practice, especially marsupialization. The most accurate and reliable method for evaluating bone formation in healing bone defects is computed elaboration of 3D radiographs.[12,31,38] Five trials have recently used this type of assessment to evaluate decompression.[12,13,18-20] One previous report, which used computerized 3D examination analysis of 15 marsupialized keratocysts, showed a 50% reduction within ~8 months, a positive correlation between volume reduction and the treatment duration, and a correlation between the daily reduction rate and the initial volume.[21] That study reported a mean period between the pre- and postoperative CT scans of 13.7 months with a wide range of 4.5 to 459.6 months. During the long-term follow-up, the lesion did not significantly decrease in size after substantial shrinkage during the first year.[21] The strength of our study was the evaluation method used for a specific treatment modality. CBCT was preferred as the examination technique owing to the good resolution and absence of distortion and the 40- to 60-fold lower exposure dose compared with multislice CT, because marsupialization requires multiple postoperative evaluations.[12,17] Although CBCT does not have the objective calibration of the gray scale, because it does not provide Hounsfield units,[39] the reliability of CBCT in the assessment of osseous consolidation has been supported as a standard in histomorphometric references.[13] The method of digital segmentation used in the present study, which has been validated as the best approach,[40] was combined with the imaging elaboration software Amira (Visage Imaging GmbH) for complex anatomic structure 3D reconstruction, mainly owing to its ability to contemporarily visualize the 3 spatial planes when defining the outlines of the lesion.[41] The weaknesses of the present study included the reduced sample size, heterogeneity of the histologic types, and heterogeneity of the patient population. Furthermore, the retrospective data collection, with different timing of the radiologic examinations, could have resulted in an overestimation of the relevance of the results. Further studies with more patients and a prospective, controlled 3D evaluation are needed.

In conclusion, marsupialization seems to positively contribute to the healing of cystic lesion-related bone defects and can be adopted independently of the demographic data of the patients and cyst features. New studies comparing marsupialization and decompression to each other and to radical enucleation could increase our understanding of the complex mechanisms behind cyst expansion and healing and facilitating the choice of the best treatment option for specific cases.

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The English in our report has been checked by at least 2 professional editors, both native speakers of English (certificate available at: http://www.textcheck.com/certificate/OPXhdf).

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