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Original Article

Selective regenerative management of jaw bone defects after cystectomy of odontogenic cysts: An ambispective cohort study

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Abstract

Objectives: To evaluate the clinical and radiological effectiveness of a selective, defect-based regenerative protocol for jaw bone defects after cystectomy of non-keratocystic odontogenic cysts and to identify factors associated with delayed bone healing.

Methods: This single-centre ambispective cohort study included 124 consecutive patients treated between 2019 and 2025. The control group (n = 58) underwent cystectomy with blood-clot healing and primary closure. The protocol group (n = 66) received defect-based reconstruction: advanced platelet-rich fibrin (A-PRF) for contained defects <2 cm³, a bone substitute with PRF for defects of 2–5 cm³, and guided bone regeneration with a resorbable collagen membrane and PRF for defects >5 cm³, cortical perforation or planned implant sites; giant cysts underwent preliminary decompression. The primary outcome was volumetric defect reduction on cone-beam computed tomography (CBCT) at 6 months.

Results: Volumetric reduction at 6 months was 74.8 ± 15.6% in the protocol group versus 58.9 ± 17.4% in controls ($p < 0.001$), and at 12 months 91.3 ± 8.9% versus 83.7 ± 12.1% ($p < 0.001$). No benefit was observed for defects <2 cm³ ($p = 0.34$), whereas the largest benefit was seen for defects >5 cm³ (87.6 ± 9.8% vs 74.2 ± 13.6%; $p = 0.001$). Postoperative infection decreased from 13.8% to 3.0% ($p = 0.044$). Baseline volume >5 cm³, cortical perforation and age >40 years independently increased the risk of incomplete healing at 12 months, whereas the protocol reduced it (odds ratio 0.41; 95% confidence interval 0.19–0.89).

Conclusions: Selective, defect-based regeneration accelerated bone healing and reduced infection compared with blood-clot healing, mainly in medium and large or wall-deficient defects. Small contained defects healed comparably without reconstruction; therefore, routine filling of every post-cystectomy cavity is not justified.

Keywords: Bone regeneration; Cone-beam computed tomography; Cystectomy; Guided bone regeneration; Odontogenic cyst; Platelet-rich fibrin

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Introduction

Odontogenic cysts are the most frequent intraosseous lesions of the jaws; in a recent series of 1,038 cases, radicular and dentigerous cysts accounted for 59.0% and 23.2% of lesions, respectively.[1] Enucleation with primary wound closure (cystectomy) remains the treatment of choice for most non-keratocystic lesions.[2] The procedure, however, leaves a bony cavity of variable volume and configuration. Many such cavities heal spontaneously, particularly when they are small and their bony walls are preserved, but the rate of reparative osteogenesis varies widely and depends on patient age, defect configuration, the affected jaw, preservation of the periosteum and thickness of the cortical plates.[3–6]

Whether the cavity should be filled remains controversial. Ettl et al. concluded that simple enucleation with blood-clot healing has a low complication rate and provides sufficient regeneration even in large defects.[2] A systematic review by Buchbender et al. of 13 studies found comparable two-dimensional bone regeneration with and without filling and, given the small number and heterogeneity of the studies, did not recommend routine filling.[3] A later systematic review concluded that bone grafts accelerate healing and improve the quality of new bone, but that their long-term superiority over spontaneous healing is unproven: without grafting, regeneration ranged from 50% to 100% at 6 months but exceeded 90% at 12 months.[7]

Recent comparative studies remain inconsistent. In a randomized trial, guided bone regeneration (GBR) with a bovine xenograft and a collagen membrane did not change cavity shrinkage at 3 months but increased it at 6 months (60.1% vs 48.6%).[8] In another randomized study, platelet-rich fibrin (PRF) combined with a synthetic bone substitute increased the 6-month osteogenesis rate from 76.1% to 92.9%,[9] and an injectable PRF–hydroxyapatite composite produced faster radiological healing than hydroxyapatite alone up to 4 months.[10] In contrast, a retrospective cohort study of maxillary radicular cysts found no significant benefit of GBR with a xenograft at 12 months (82.0% vs 75.2%),[11] and a randomized trial of an albumin gel–PRF mixture showed no difference from the natural blood clot in residual cavity volume or density at 6 months.[12]

Data on spontaneous healing also argue against a uniform approach. Ihan Hren and Miljavec showed that large mandibular defects regenerated spontaneously in all 33 patients studied, reaching 88% of the density of the surrounding bone, although larger defects and older age were associated with poorer healing.[4] Volumetric studies have since reported a spontaneous healing ratio of approximately 73.5% at 12 months, with residual defects in cysts larger than 3 cm³ comparable in volume to entire small cysts,[6] and residual cavity volumes in large cystic lesions of 21.1% at 6 months and 15.9% at 12 months, strongly influenced by initial lesion size.[13] For very large lesions, decompression or marsupialization before definitive enucleation reduces lesion volume and surgical morbidity.[14,15] Odontogenic keratocysts require a separate algorithm, because recurrence

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control rather than bone regeneration determines the choice of treatment.[16,17]

These data suggest that the decision to fill a post-cystectomy defect should be individualized according to defect volume, configuration, cortical integrity and plans for implant rehabilitation. In Uzbekistan, osteoplastic materials are increasingly used after cystectomy,[18] but the effect of a selective, defect-based protocol has not been evaluated. The aim of this study was to assess the clinical and radiological effectiveness of a differentiated, defect-based regenerative protocol after cystectomy of non-keratocystic odontogenic cysts and to identify factors associated with delayed bone healing.

Methods

Study design and setting

This single-centre ambispective cohort study was conducted at Tashkent State Medical University, Tashkent, Uzbekistan. Consecutive patients treated between 2019 and 2025 were included (Figure 1). Patients treated before the introduction of the defect-based regenerative protocol formed the control group (retrospective component), and those treated after its introduction formed the protocol group (prospective component). Reporting follows the STROBE statement.19

Participants

Patients aged 18 years or older were eligible if they had a histologically verified non-keratocystic odontogenic cyst of the maxilla or mandible, a post-cystectomy bone defect confirmed intraoperatively and on cone-beam computed tomography (CBCT), and at least 12 months of follow-up. Exclusion criteria were odontogenic keratocyst, tumour-like lesions, uncontrolled diabetes mellitus, active osteomyelitis, bisphosphonate-associated bone lesions and incomplete radiological follow-up.

Sample size

No a priori sample size calculation was performed, because all consecutive eligible patients treated during the study period were included. With 58 and 66 patients, the study had 90% power to detect a between-group difference of 10 percentage points in 6-month volumetric reduction, assuming a standard deviation of 17% and a two-sided α of 0.05.

Interventions

In the control group (n = 58), the cavity was left to heal under a blood clot and the wound was closed primarily. In the protocol group (n = 66), one of three reconstruction options was selected according to defect volume and configuration: (i) advanced platelet-rich fibrin (A-PRF) alone for contained defects smaller than 2 cm³ with preserved walls; (ii) a bone substitute combined with PRF for defects of 2–5 cm³; and (iii) GBR with a resorbable collagen membrane and PRF for defects larger than 5 cm³, defects with thinned or perforated cortical plates and defects at sites of planned implant placement. PRF was prepared from autologous venous blood. In patients with giant cysts, decompression was performed as a first stage before definitive cystectomy.

Surgical procedure

All procedures followed the same principles: elevation of a full-thickness mucoperiosteal flap, complete removal of the cyst lining, careful curettage of the cavity and meticulous haemostasis. Causative teeth associated with radicular cysts received endodontic treatment according to a uniform clinical protocol. Postoperative care, antibiotic prophylaxis and analgesia were comparable between groups. All specimens were examined histologically.

Outcome variables and measurements

CBCT was performed 1–3 days after surgery and at 6 and 12 months. Defects were segmented using the same software, and the initial cavity volume, residual volume and relative volumetric reduction, calculated as $(V0 - Vt)/V0 \times 100\%$, were determined. Because CBCT grey values are not equivalent to Hounsfield units,20,21 regenerate quality was expressed as the ratio of the mean grey value of a region of interest within the defect to that of a symmetrical intact region of the same jaw.

The primary outcome was volumetric defect reduction at 6 months. Secondary outcomes were volumetric reduction at 12 months; relative regenerate density at 12 months; complete wound epithelialization by day 14; pain on a 10-point visual analogue scale (VAS) on day 7; postoperative infection requiring re-intervention; wound dehiscence; transient neurosensory disturbance in the inferior alveolar nerve territory; retention of adjacent teeth at 12 months; and readiness of the site for implant placement within 9 months in patients planning implant rehabilitation.

Statistical analysis

Statistical analyses were performed with SPSS version 27 (IBM Corp., Armonk, NY, USA). Normality was assessed with the Shapiro–Wilk test. Continuous variables were compared with Student's t-test or the Mann–Whitney U test, as appropriate. Categorical variables were compared with Pearson's χ^2 test, or with Fisher's exact test when any expected cell count was below 5. Changes over time were analysed with a linear mixed model. Factors associated with incomplete bone healing at 12 months were identified by multivariable logistic regression and are presented as odds ratios (OR) with 95% confidence intervals (CI). A two-sided $p < 0.05$ was considered statistically significant.

Results

Participants

The study included 124 patients (68 men and 56 women) aged 18–67 years. The groups did not differ significantly in age, sex, affected jaw, cyst type, baseline defect volume, proportion of defects larger than 5 cm³ or cortical perforation (Table 1).

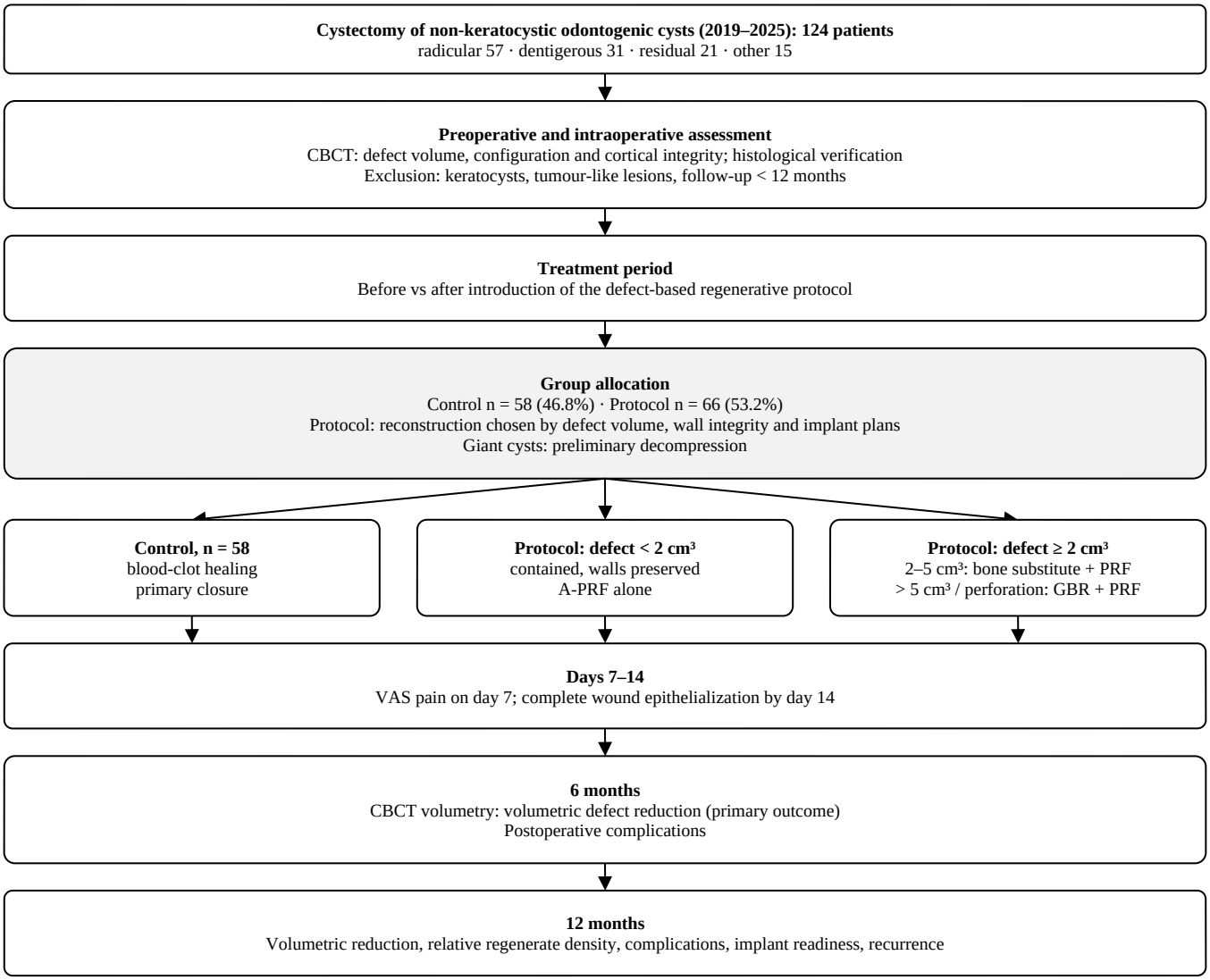


Figure 1: Study design and follow-up points. A-PRF, advanced platelet-rich fibrin; CBCT, cone-beam computed tomography; GBR, guided bone regeneration; PRF, platelet-rich fibrin; VAS, visual analogue scale.

Table 1: Baseline characteristics of the study groups.

Characteristic	Control (n = 58)	Protocol (n = 66)	p
Age, years, mean ± SD	36.1 ± 11.9	35.2 ± 12.7	0.69[a]
Sex, male/female, n	31/27	37/29	0.77[b]
Jaw, mandible/maxilla, n	35/23	37/29	0.63[b]
Cyst type, n (%)			>0.99[b]
Radicular	27 (46.6)	30 (45.5)	
Dentigerous	14 (24.1)	17 (25.8)	
Residual	10 (17.2)	11 (16.7)	
Other non-keratocystic	7 (12.1)	8 (12.1)	
Defect volume, cm³, mean ± SD	4.8 ± 2.1	5.0 ± 2.3	0.62[a]
Defect volume > 5 cm³, n (%)	18 (31.0)	21 (31.8)	0.92[b]
Cortical perforation, n (%)	13 (22.4)	15 (22.7)	0.97[b]

[a]Student's t-test; [b]Pearson's χ^2 test. SD, standard deviation.

Early clinical outcomes

Complete wound epithelialization by day 14 was achieved in 46 of 58 control patients (79.3%) and 61 of 66 protocol patients (92.4%; p = 0.034). The median VAS pain score on day 7 was 3 (interquartile range [IQR] 2–4) in the control group and 2 (IQR 1–3) in the protocol group (p = 0.018) (Table 2).

Table 2: Clinical and radiological outcomes.

Outcome	Control (n = 58)	Protocol (n = 66)	p
Complete wound epithelialization by day 14, n (%)	46 (79.3)	61 (92.4)	0.034[a]
VAS pain on day 7, median (IQR)	3 (2–4)	2 (1–3)	0.018[b]
Volumetric defect reduction at 6 months, %, mean ± SD	58.9 ± 17.4	74.8 ± 15.6	<0.001[c]
Volumetric defect reduction at 12 months, %, mean ± SD	83.7 ± 12.1	91.3 ± 8.9	<0.001[c]
Relative regenerate density at 12 months, mean ± SD	0.79 ± 0.10	0.87 ± 0.08	<0.001[c]

Outcome	Control (n = 58)	Protocol (n = 66)	p
Postoperative infection requiring re-intervention, n (%)	8 (13.8)	2 (3.0)	0.044[d]
Wound dehiscence, n (%)	7 (12.1)	3 (4.5)	0.187[d]
Transient neurosensory disturbance, n (%)	5 (8.6)	3 (4.5)	0.472[d]
Adjacent teeth retained at 12 months, n (%)	49 (84.5)	62 (93.9)	0.086[a]
Implant site ready within 9 months, n/N (%)	9/21 (42.9)	16/21 (76.2)	0.028[a]
Recurrence within 12 months, n	0	0	–

[a]Pearson's χ^2 test; [b]Mann–Whitney U test; [c]Student's t-test; [d]Fisher's exact test. IQR, interquartile range; SD, standard deviation; VAS, visual analogue scale.

Radiological outcomes

At 6 months, the mean volumetric defect reduction was 58.9 ± 17.4% in the control group and 74.8 ± 15.6% in the protocol group (p < 0.001), a difference of 15.9 percentage points. At 12 months, the corresponding values were 83.7 ± 12.1% and 91.3 ± 8.9% (p < 0.001), and the difference had narrowed to 7.6 percentage points (Figure 2; Table 2). Relative regenerate density at 12 months was higher in the protocol group (0.87 ± 0.08 vs 0.79 ± 0.10; p < 0.001).

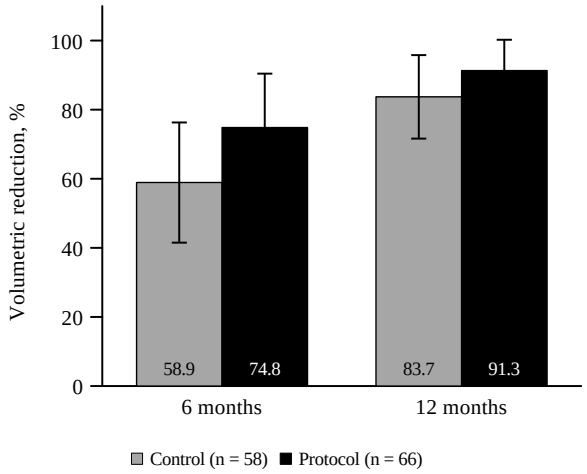


Figure 2: Volumetric reduction of the post-cystectomy defect at 6 and 12 months in the control group (blood-clot healing, n = 58) and the regenerative protocol group (n = 66). Mean ± SD; Student's t-test, p < 0.001 at both time points.

The effect depended on baseline defect volume (Figure 3; Table 3). For contained defects smaller than 2 cm³, the 12-month volumetric reduction did not differ between groups (95.1 ± 4.2% vs 92.6 ± 5.8%; p = 0.34). For defects of 2–5 cm³, it was 92.8 ± 7.1% in the protocol group and 84.1 ± 10.9% in controls (p = 0.006), and for defects larger than 5 cm³, 87.6 ± 9.8% and 74.2 ± 13.6%, respectively (p = 0.001).

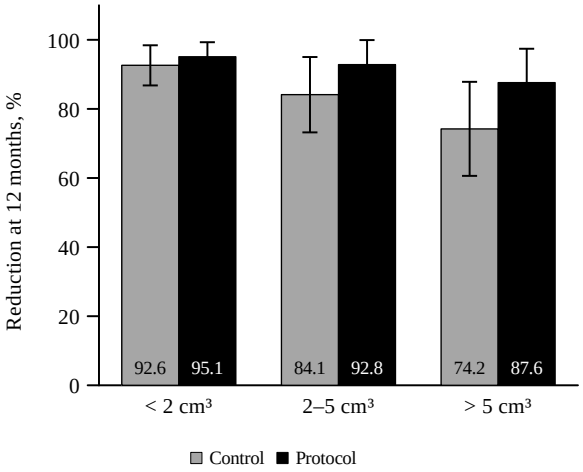


Figure 3: Volumetric defect reduction at 12 months according to baseline defect volume. Mean ± SD; Student's t-test: < 2 cm³, p = 0.34; 2–5 cm³, p = 0.006; > 5 cm³, p = 0.001.

Table 3: Volumetric defect reduction at 12 months according to baseline defect volume.

Baseline defect volume	Control	Protocol	p
Reduction at 12 months, %	92.6 ± 5.8	95.1 ± 4.2	0.34
Reduction at 12 months, %	84.1 ± 10.9	92.8 ± 7.1	0.006
> 5 cm³, n	18	21	
Reduction at 12 months, %	74.2 ± 13.6	87.6 ± 9.8	0.001

Mean ± SD; Student's t-test.

Complications and rehabilitation

Postoperative infection requiring re-intervention occurred in 8 control patients (13.8%) and 2 protocol patients (3.0%; p = 0.044). Wound dehiscence (12.1% vs 4.5%; p = 0.187) and transient neurosensory disturbance (8.6% vs 4.5%; p = 0.472) were also less frequent in the protocol group, but these differences were not statistically significant. No recurrences were observed during 12 months of follow-up (Table 2; Figure 4).

Among 42 patients planning delayed implant rehabilitation (21 per group), the site was ready for implant placement within 9 months in 9 control patients (42.9%) and 16 protocol patients (76.2%; p = 0.028). Adjacent teeth were retained at 12 months in 49 of 58 (84.5%) and 62 of 66 (93.9%) patients, respectively (p = 0.086).

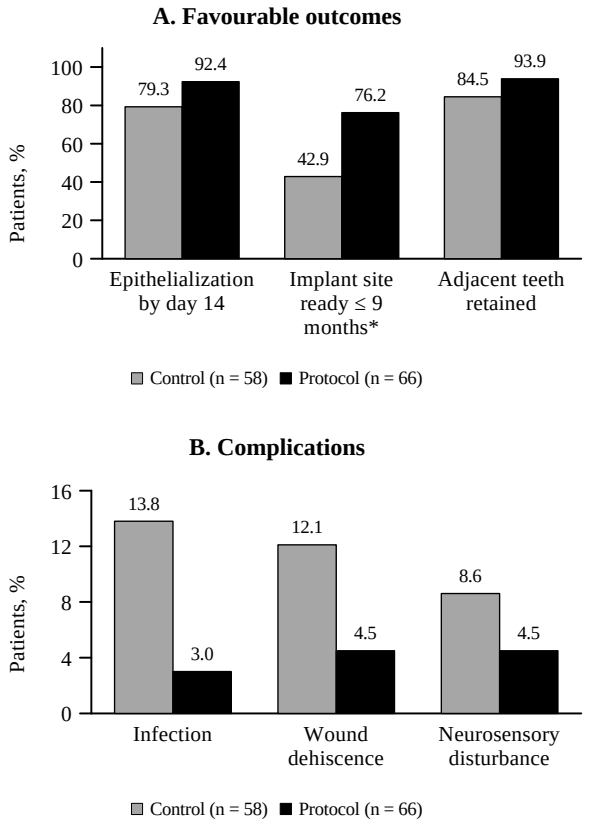


Figure 4: Favourable clinical outcomes (A) and complications (B) in the control group (n = 58) and the regenerative protocol group (n = 66), % of patients. *Assessed in 42 patients planning implant rehabilitation (21 per group). Pearson's χ^2 test in panel A; Fisher's exact test in panel B.

Factors associated with incomplete bone healing

In multivariable logistic regression, the risk of incomplete bone healing at 12 months increased with baseline defect volume above 5 cm³ (OR 3.42; 95% CI 1.56–7.48), cortical perforation (OR 2.67; 95% CI 1.18–6.03) and age above 40 years (OR 1.94; 95% CI 1.01–3.71), whereas treatment according to the regenerative protocol was associated with a lower risk (OR 0.41; 95% CI 0.19–0.89) (Table 4).

Table 4: Factors associated with incomplete bone healing at 12 months (multivariable logistic regression).

Factor	OR (95% CI)	p
Defect volume > 5 cm³	3.42 (1.56–7.48)	0.002
Cortical perforation	2.67 (1.18–6.03)	0.018
Age > 40 years	1.94 (1.01–3.71)	0.046
Regenerative protocol (vs blood-clot healing)	0.41 (0.19–0.89)	0.024

CI, confidence interval; OR, odds ratio.

Discussion

In this cohort, a selective, defect-based regenerative protocol accelerated bone healing after cystectomy, improved regenerate density and reduced postoperative infection compared with blood-clot healing. The benefit was concentrated in medium and large defects, whereas small contained cavities reached comparable 12-month outcomes without reconstruction. These findings support selective rather than universal regenerative surgery after cystectomy.

Our results are consistent with the available comparative evidence. The early advantage at 6 months agrees with the randomized trials of Shi et al. and Li et al.,[8,9] and the narrowing of the between-group difference from 15.9 to 7.6 percentage points by 12 months mirrors the pattern described in a systematic review, in which grafts mainly accelerate healing while spontaneous regeneration catches up over time.[7] The absence of a 12-month benefit of a xenograft in maxillary radicular cysts[11] and of an albumin gel–PRF mixture in a randomized trial[12] may partly reflect defect selection: in our study, small contained defects, which were treated with A-PRF alone, likewise showed outcomes comparable with blood-clot healing. The 12-month reduction in the control group (83.7%) is within the range reported for unfilled defects in volumetric studies.[6,13]

Defect size emerged as the main effect modifier. Larger preoperative cyst volume was associated with poorer bone formation in randomized and cohort studies,[8,11,13] and large cysts leave residual defects of clinically relevant volume.[6] In our study, the advantage of the protocol increased from a non-significant 2.5 percentage points in defects smaller than 2 cm³ to 13.4 percentage points in defects larger than 5 cm³, and defect volume above 5 cm³ and cortical perforation were the strongest independent predictors of incomplete healing. Older age was also an independent risk factor, in line with earlier observations of slower spontaneous healing in older patients.[4,6]

Spontaneous healing therefore remains a valid option. Small contained cavities with preserved cortical walls in younger patients can heal without costly materials,[4,6] whereas through-and-through defects, marked thinning or perforation of the cortical plates and sites of planned implant placement represent a different clinical situation. The higher proportion of sites ready for implant placement within 9 months (76.2% vs 42.9%) is clinically relevant because it shortens the overall rehabilitation period.

The lower infection rate in the protocol group may reflect stabilization of the blood clot and reduction of dead space by PRF and graft material. However, because the control group was historical, changes in perioperative care over time cannot be excluded as a contributing factor. Evidence on PRF in cystic cavities is still dominated by case reports and small series,[22] and PRF alone did not outperform the natural clot in a randomized trial.[12] Because the protocol combined several components, our data cannot attribute the effect to any single one.

Assessment methodology also matters. Two-dimensional panoramic radiography poorly reflects the volume and configuration of a defect, whereas CBCT volumetry allows standardized three-dimensional comparison of healing strategies.[5,6,8,11] CBCT grey values correlate only moderately with Hounsfield units and depend on the device and acquisition settings,[20,21] which is why regenerate quality was expressed as a ratio to a symmetrical intact region rather than in absolute density units.

Odontogenic keratocysts were excluded because their reconstruction cannot be considered separately from recurrence risk; simple enucleation is associated with the highest recurrence rates, whereas adjuvant and staged approaches change the prognosis.[16,17] Other options, such as recombinant human bone morphogenetic protein-2,[23,24] autogenous tooth-derived grafts[25] and three-dimensionally printed scaffolds,[26] are supported in this indication only by small series or preclinical data and require comparative clinical evaluation.

This study has limitations. It was a single-centre, non-randomized study with a historical control group, so temporal changes in surgical experience and perioperative care may have influenced the results. Within the protocol group, the reconstruction technique was chosen according to defect characteristics, which precludes comparisons between individual

techniques. Follow-up was limited to 12 months, and costs were not analysed. Nevertheless, the design reflects real clinical practice, in which the decision to fill a defect is based on anatomical and rehabilitation factors rather than applied uniformly.

Conclusions

A differentiated, defect-based regenerative protocol after cystectomy of non-keratocystic odontogenic cysts accelerated bone healing and reduced postoperative infection compared with blood-clot healing. The benefit was greatest in defects larger than 2 cm^3, in defects with thinned or perforated cortical plates and at sites of planned implant placement. Small contained defects with preserved walls healed comparably without reconstruction, so routine filling of every post-cystectomy cavity cannot be considered optimal. Prospective randomized studies with standardized CBCT volumetry and separate analysis of radicular, dentigerous and residual cysts are needed.

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Conflict of interest

The author has no conflict of interest to declare.

Authors' contributions

Niginabonu A. Sadullaeva: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. The author has critically reviewed and approved the final draft and is responsible for the content and similarity index of the manuscript.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author used Claude (Anthropic) to translate the manuscript into English, edit the language and prepare tables and figures. After using this tool, the author reviewed and edited the content as needed and takes full responsibility for the content of the publication.

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