

Original Article

A Multicenter Retrospective Case Review of Outcomes and Complications of S53P4 Bioactive Glass

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OBJECTIVE: The objective of this multicenter retrospective case review was to assess the natural clinical course, efficacy, and safety of mastoid obliteration with S53P4 Bioactive Glass (bioactive glass).

METHODS: Retrospective case note review in a regional Tertiary Referral Centre and District General Hospital. Patients undergoing mastoid cavity obliteration as part of primary or secondary procedure with bioactive glass between 2012 and 2018. Outcome measures were assessed from a prospectively collated database and case note review. Primary outcomes were the common morbidities of a mastoid cavity; dry or discharging ear (Merchant's scale), vertigo in cold air, and a watertight middle ear. Patients were also assessed for audiological outcomes and recidivism.

RESULTS: Ninety patients were included. During the follow-up period, (mean, 22 months; range, 6–59 months) cholesteatoma recidivism was observed in 2% of ears (2 patients). An acceptably dry (Merchant Grade 0–1) ear was achieved in 91% of all ears (95% primary cases, 80% secondary cases). Delayed healing of the graft in the external ear canal retaining the S53P4BAG Bioactive Glass (BonAlive Ö (BonAlive Ö Biomaterials Ltd., Turku, Finland)) within the mastoid occurred in 13% (12 ears). However, in all cases, conservative management resulted in complete healing.

CONCLUSIONS: Bioactive glass provides a safe and effective means of mastoid obliteration. Complications including overlay graft failure and slow epithelialization, resulting in prolonged postoperative discharge (up to 2 months) and dehiscence into the external ear canal, do not preclude full recovery and may be successfully managed conservatively.

KEYWORDS: Cholesteatoma, mastoid, mastoidectomy, obliteration

INTRODUCTION

The “Front-to-Back” approach to cholesteatoma surgery is widely utilized. It minimizes the destruction of disease-free mastoid, and allows for early surgical identification of the integrity of the ossicular chain and other important anatomical structures. Despite these advantages, the resulting canal wall defect presents a challenge to the surgeon. The defect enlarges with extent of surgery, from atticotomy, to atticostomy, and modified radical mastoidectomy; M2a, M2b, and M2c in the International Otology Outcomes Group consensus statement.¹ The surgeon must decide upon the management of these defects intraoperatively using their clinical acumen and knowledge of the patient's lifestyle and wishes. There are many different means by which a mastoid cavity may be obliterated. There are a number of techniques that have been utilized to facilitate this outcome: cartilage to reconstruct the canal wall, bone dust or chips harvested intraoperatively, or a variety of muscular flaps and synthetic substances (bioactive glass, hydroxyapatite, titanium, or silicone) to obliterate the mastoid cavity.^{2–4}

The morbidity to the patient of a mastoid cavity—including dizziness on exposure to cold air, being prone to more frequent infections, potential lifelong attendance at outpatient departments, and the associated burden to the service of providing such care—are far from insignificant. Thus, both the patient and the clinical service benefit from obliteration of the mastoid cavity. In a recent study, obliteration of the mastoid has been shown to reduce disease recurrence in children.⁵

S53P4BAG Bioactive Glass (BonAlive Ò, (BonAlive Ò Biomaterials Ltd., Turku, Finland)) (bioactive glass), is a silica-based biomaterial, composed of silicon dioxide, sodium oxide, calcium oxide, and phosphorous pentoxide. Bioactive glass has several properties that are advantageous, which led to its use in mastoid obliteration. It is both osteoconductive (it provides a framework for bone growth), and osteopductive (it stimulates bone growth).⁶ It has also been demonstrated to have antibacterial properties against a wide range of microorganisms.⁷⁻⁹ There have been several studies published relating to the safety, anatomical and functional features, and quality of life relating to the use of bioactive glass.¹⁰⁻¹² However, there is a paucity of evidence on the clinical applications of bioactive glass, their complications, and their management. The aim of this retrospective case review was to identify the techniques and the outcomes achieved when bioactive glass is used to obliterate the mastoid. Data relating to these issues covers the consent, shared decision making with our patients, and intraoperative decision making.

MATERIALS AND METHODS

Study Design

Consultant Otolaryngology-Head and Neck Surgeons working in Northern Ireland, with subspecialist interest in Otology, were asked to identify patients for this retrospective case review through their prospectively-recorded surgical logbook. Where the respective surgeons questioned the completeness of the data, the search terms "Obliteration" and "Mastoid Obliteration" were augmented by a search for all patients who had undergone "modified radical mastoidectomy."

Methods

Retrospective case note review of both physical and electronic health care records. Patient notes were reviewed to identify demographics, surgical details including confirmation of the use of bioactive glass, presence or absence of complications of open cavity surgery (dry ear (Merchant's scale 0-1, vertigo in cold air, watertight ear), audiological outcomes, and recurrence.¹³ Patients with less than 6 months clinical follow-up were excluded. Data was collated in a spreadsheet prior to statistical analysis using RStudio software (R Core Team, 2018).

RESULTS

Four surgeons working in 2 different otolaryngology departments identified 90 patients with adequate follow-up and complete data sets who had undergone procedures utilizing bioactive glass. Bioactive glass was used to obliterate mastoid cavities in 55 primary procedures and 35 secondary procedures. Fifty-seven ears were approached using a postaural soft tissue approach, 33 via an end-aural approach. Table I shows the classification of cases in both primary and secondary obliteration. The patients had a median age of 38 years (range, 10-88 years), with gender and operative-side ratio 1 : 1. Median follow-up at time of data collection was 15.5 months (range, 6-65 months).

Operative Findings and Details

Ossicular status, as recorded in the operative notes, was graded using the Mills Staging System,¹⁴ from 0 (chain intact) to 3 (erosion of the malleus, incus, and stapes arch). In 23 cases, the ossicular status was could not be determined. In some cases, this was because the middle ear was not entered during a secondary obliteration ($n = 14$) or

revision surgery; and in others, because clear documentation was not available at the time of note review ($n = 9$). The chi-squared test was used to look for greater representation of one ossicular status over the others, and none was found ($P = .78$). Table II shows the number of cases at each ossicular Mills status. Forty-one patients underwent ossiculoplasty, the most common means of reconstruction being cartilage reinforced Type III ($n = 17$), or the use of Titanium Partial ($n = 12$), or Total Ossicular Reconstruction Prosthesis ($n = 5$).

The 7th cranial nerve (facial) was found to have been exposed as a result of disease in 8 cases. In 6 of these cases, the horizontal nerve was exposed; and in 2 more, the vertical segment was dehiscence. In the latter 2 cases, the nerve was covered with temporalis fascia prior to the application of bioactive glass. A fistula in the lateral semicircular canal was present in 5 cases. A further 7 patients were found to have both an exposed facial nerve and a fistula in the lateral semicircular canal. The presence of both facial dehiscence and lateral semicircular canal fistula in such a high proportion of patients highlights the need for intraoperative vigilance, in particular where one dehiscence has already been identified. At the time of publication, no patient had suffered delayed complications resulting from the use of bioactive glass in the presence of a labyrinthine or facial nerve dehiscence.

A number of different graft materials were used for both the tympanic membrane repair and as a covering for the bioactive glass. The covering graft prevents the bioactive glass from extruding into the external auditory canal, and provides a framework for epithelial growth, as an autograft (Figure 1).

Postoperative Outcomes

The diversity of procedures, ossicular status, and the objective of this paper being to assess the use and clinical outcomes of bioactive glass mean that neither subgroup analysis of audiological outcomes nor formal analysis of recidivism have been performed. However, the median change in the air-bone gap between pre- and post- (>6 months) operative audiometry was 1 dB (range, -36 dB to +25 dB). Thirty-one patients showed a change within the margin of error for audiometry (± 5 dB), while 19 had a lower hearing threshold postoperatively, and 21 had a higher hearing threshold postoperatively. We did not aim to assess the impact of obliteration on hearing outcomes within this retrospective study. Where the ossicular status was recorded, it did not preclude a decision to make use of bioactive glass, nor did the bioactive glass preclude the performance of an ossiculoplasty. At the time of publication, no patient has demonstrated recurrence. Six (7%) patients have demonstrated retraction of the attic, one of whom has undergone exploratory tympanotomy where a suspicious area was found to be scar tissue rather than a cholesteroloma pearl.

Clinical complications of open cavity surgery (dependence on clinical staff for aural toilet, discharging cavity, vertigo in cold air, and need to protect the ear from water) are shown in Figure 2. Seven of the 90 (8%) patients had intermittently discharging ears at the time of last follow-up (1 as a result of ventilation tube) The remaining 83/90 (92%) had a dry ear. Eighteen (20%) (10 primary, 8 secondary) reported the presence of discharge and attended the outpatient department frequently for 6 weeks postoperatively. This was due to delayed healing of the graft covering of the bioactive

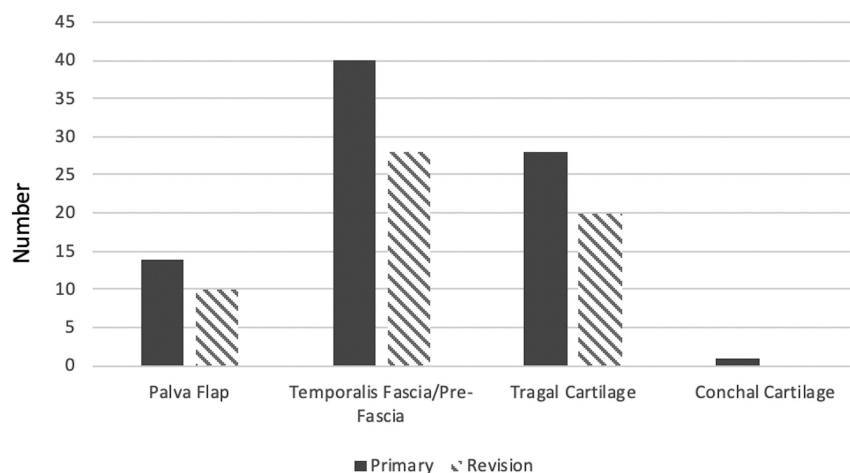


Figure 1. Frequency of covering graft material in primary and secondary obliteration.

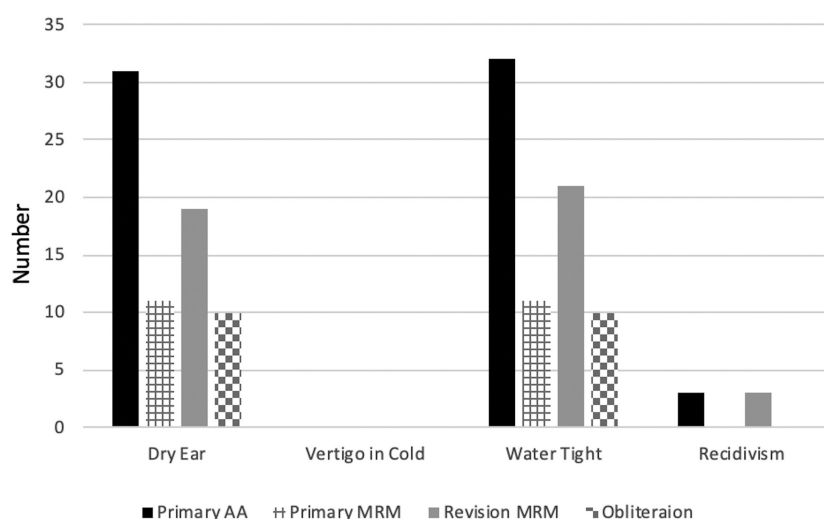


Figure 2. Frequency of common complications of mastoid cavity in patients who have undergone mastoid obliteration with bioactive glass. AA, atticostomy; MRM, modified radical mastoidectomy.

glass, and in all cases, responded to regular microsuction and topical applications of antibiotic and steroid ointments. None of the 90 (0%) suffered from vertigo on exposure to cold air, and 1/90 (1%) did not have a watertight ear as a result of the insertion of a ventilator tube. All healed without deleterious effect on the mastoid obliteration. Further complication was seen in the occurrence of surgical site infection in 2/90 (2%) cases, both of whom resolved with oral and topical antibiotic treatment. One patient out of the 90 (1%) failed to comply with follow-up and attended a solitary review at more than 6 months postoperatively. She had suffered prolonged discharge from the ear that had settled a few weeks prior to review. There had been complete loss of the bioactive glass and covering graft tissue but she had been left with a well healed and dry mastoid cavity.

DISCUSSION

Within the limits of the current study, bioactive glass provides a safe and effective means of mastoid obliteration. We report outcomes in a group of patients who have undergone mastoid obliteration as an adjunct to a diverse group of procedures. Complications of the procedure are rare and outcomes good, irrelevant of surgical approach

to initial mastoid surgery and concurrent procedures. While concurrent or previous procedures may impact on the choice of covering graft, the most common complication suffered by patients is an increased frequency of attendance in the initial healing phase, for ear dressing. This is to facilitate epithelialization of the graft covering the bioactive glass.

Skoulakis et al. identified 9 papers where bioactive glass had been utilized in mastoid obliteration.¹⁵ As in our study, the application of bioactive glass in these studies was not uniform and between them included 199 cases. Neither rate of infection in our study (7/90, 8%) and the summarized data (23/199, 12%) (Fisher's exact test, $P = .53$), nor rates of postoperative vertigo differ (Fisher's exact test, $P = .53$). Our data indicate a higher rate of prolonged healing (18/90, 20%) as opposed to the rate (10/199, 5%) in the summarized data (Fisher's exact test, $P < .05$). This may be due to the inclusion of canal wall-up cavity obliterations in some of the summarized data. Furthermore, there is both a lack of standardization in both operative technique and categorization of postoperative findings. These challenges mean that prospective study against other techniques and materials is required.

Table 1. Surgery Performed in Primary and Secondary Procedures Prior to Obliteration

Primary Procedures		Secondary Procedures		
MRM (Back-Front)	Atticoantrostomy	MRM (Back-Front)	Atticotomy/Atticoantrostomy	Obliteration
14	41	12	13	10

Where dehiscence of the lateral semicircular canal had occurred, surgical decision making was uniform in that all patients had a periosteal or fascial graft placed over the dehiscence prior to application of bioactive glass. In contrast, in some cases, bioactive glass was placed directly upon the dura and facial nerve in the event of their exposure. The duration of follow-up is widely varied within our population. However, it is reassuring to note that none of these patients have had any late complications (hearing loss, vertigo, or facial palsy) arising as a result of the obliteration, during the follow-up period.

The issues of recurrence and recidivism have impacted upon the surgical technique used in obliterating the mastoid cavity. In the first few patients receiving bioactive glass, the grafts were placed with the temporalis fascia or muscular flaps providing both tympanic and covering grafts. In some of these early patients, the attic has retracted (Image 1). Our practice takes a number of measures to facilitate a successful obliteration and to attempt to prevent the position of clinical equipoise presented by a new retraction pocket in a previously operated ear. First, when performing the mastoidectomy, the facial ridge is only lowered as far as required to ensure disease clearance. This is another advantage to the front-back approach, which was already preferred by surgeons reporting in this paper (Table 1). Second, when performing the reconstruction and obliteration, a small attic cavity is lined with a temporalis fascia graft, prior to using tragal cartilage to seal off the mastoid cavity from the attic and middle ear space. The mastoid may then be filled with bioactive glass and covered appropriately. Once healed, the small attic cavity (Image 2) is easily examined and cleaned, should cleaning prove necessary. The retention of a small attic cavity and high facial ridge reduces the surface area of the covering graft. However, it has not obviated the problem of getting such a large graft to heal in the external ear canal. There have been a number of pedicled flaps described, utilized in mastoid obliteration.³ The small number of local flaps utilized as part of our series precludes comment on the efficacy when utilizing bioactive glass.

CONCLUSION

Patients receiving bioactive glass have a greater than 90% chance of having a postoperative ear free of troublesome symptoms associated with mastoid cavities. They should be aware of the frequent (1/5, 20%) requirement for close follow-up in the 6 weeks following surgery.

The current practices and techniques of surgeons beginning to make use of bioactive glass will likely determine both their patient and

technique selection. Where a surgeon is confident in their disease clearance, primary obliteration may be undertaken. However, the long-term benefits of reduced attendance at the outpatient department may just as well be achieved through a secondary procedure, at which time disease clearance may be confirmed. In secondary procedures, the potential to utilize the epithelium of the mastoid cavity, with its subdermal blood supply to cover the obliteration, is appealing but often impractical. The choice of grafts and flaps used during the obliteration will also likely depend upon the experience of the individual surgeon and indeed on what is available following previous procedures.

Bioactive glass provides a safe and effective means of mastoid obliteration. The role of obliteration in prevention of recurrence, the mechanism of its benefit, and the clinical outcomes achieved require further prospective study.

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Table 2. Ossicular Status of Ears Undergoing Exploration of the Middle Ear

	Mills Ossicular Status				
	0	1	2	3	Not Recorded
Number of Cases	16	17	22	12	23

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