

The Safety and Efficacy of Hydroxyapatite Repair of Cholesteatoma Skull Base Defects

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Abstract

Objective. To investigate the possibility of hydroxyapatite as a safe and effective alternative to currently used bioavailable materials for repair of tegmen defects and labyrinthine fistulas in the setting of cholesteatoma.

Study Design. Retrospective study.

Setting. Tertiary-level-care hospital.

Methods. Electronic medical records of patients 18+ years undergoing cholesteatoma-removal surgery between 2013 and 2022 were reviewed.

Results. Twenty-two patients diagnosed with cholesteatoma who underwent repair of either a tegmen defect or labyrinthine fistula using hydroxyapatite were evaluated. There were 17 canal wall up (CWU) and 5 canal wall down (CWD) surgeries. The cholesteatoma recidivism rate was 18.2% (n = 4) and the recurrence rate was 4.5% (n = 1). To ensure that these rates were similar to cholesteatoma-removal surgeries in which hydroxyapatite was not used, a 22 age, gender, and operative technique-matched cohort was evaluated. For patients with CWU surgeries, the rate of recurrence and recidivism were identical between both cohorts (0% and 23.5%, respectively; $P = 1$ for both). While in CWD surgeries, there was a nonstatistically significant difference in the recurrence as there was only 1 patient with recurrence in the hydroxyapatite group ($P = 1$). Three (13.5%) patients in the hydroxyapatite group had a local infection and 1 (4.5%) had a subacute mastoid infection. All patients with semicircular canal fistulas had consistent bone lines on postoperative audiograms, with no worsening sensorineural hearing loss.

Conclusion. In our cohort, hydroxyapatite was safe and successful in repairing skull base defects and inner-ear fistulas in the setting of cholesteatoma with a low rate of postoperative infection and no evidence of a higher rate of cholesteatoma recurrence. Further studies are needed to assess population generalizability.

Keywords

cholesteatoma, efficacy, hydroxyapatite, safety, skullbase defects

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Cholesteatoma is known to be a surgically challenging chronic otologic disease with an incidence of 3 to 15 per 100,000 person-years.¹ Cholesteatoma is associated with bony erosion which can be extensive involving tegmen defects, cerebrospinal fluid (CSF) leaks, or the creation of labyrinthine fistulas.² To reconstruct these defects, surgeons have traditionally used autologous materials such as cartilage, fascia, or bone pâté.³ However, these are not always robustly accessible especially in cases of large defects or revision surgeries. Furthermore, the use of synthetic materials, such as hydroxyapatite cement, is gaining popularity in skull-base surgery.

The use of hydroxyapatite has previously been investigated in lateral skull repairs of intraoperative CSF leaks.⁴ Kveton and colleagues were one of the first to investigate hydroxyapatite and its utility in to repair CSF leaks in a variety of pathological settings.⁵⁻⁷ Our research group continued to explore this question and investigated patient characteristics that make for ideal candidates for hydroxyapatite repair.⁸

Recent studies have shown that hydroxyapatite is a safe and effective material for this purpose and can be used in lieu of autologous materials, with postoperative complication rates ranging from 0% to 8%.^{9,10} Utilization of hydroxyapatite in cases with cholesteatoma, has only been described as a material employed for mastoid obliteration in mastoidectomy surgery. No study has evaluated the use of hydroxyapatite for

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skull-base defect and labyrinthine fistula repair in the setting of cholesteatoma.

To our knowledge, this is the first study to examine the use of hydroxyapatite for tegmen and semicircular canal defect repair caused by cholesteatoma. Herein, we investigate the safety and efficacy of utilizing this synthetic material when treating a disease that carries the risk of secondary infection and significant inflammatory response, within our institutional cohort.

Methods

This study was deemed exempt by the Human Research Protection Program Institutional Review Board at our institution. Retrospective chart review from 2013 to 2022 was performed at our institution. Patients 18 years or older with a cholesteatoma-induced tegmen defect and concomitant CSF leak or labyrinthine fistula deemed to require repair by the surgeon were eligible for study inclusion. Patients undergoing surgical treatment for cholesteatoma in which hydroxyapatite was utilized to repair defects of the skull base were reviewed after identifying cases using Current Procedural Terminology codes (69635-69637, 69641-69646, 61591, 62100). To isolate the effect of hydroxyapatite on safety and efficacy of cholesteatoma treatment, we examined a randomly selected group of patients 18+ years with a diagnosis of cholesteatoma with skull base defect whose resulting defects were repaired using temporalis fascia grafts.

We reviewed the operative notes of all the identified patients with cholesteatoma-induced skull base defects that were repaired with cement. When reviewing the operative notes, we identified 10 patients who had cholesteatoma-induced lateral semicircular canal fistulas which were repaired via cement as well. Preoperative and postoperative audiograms were evaluated to assess the successful repair of labyrinthine fistulas. Additionally, all patients received imaging via computed tomography scan preoperatively. In 2 of these patients, the fistula was identified preoperatively, and in the remaining, the fistula was identified intraoperatively.

The medical record review was conducted to obtain patient demographic information, surgical variables, and outcome details. Demographic information included sex, age, body mass index, race, insurance status, and smoking status. Surgical variables included the side of surgery, and surgical technique used (canal wall up [CWU] vs canal wall down [CWD] tympanomastoidectomy). Outcomes assessed include infection rate including superficial and subacute infections and revision rates. Specifically, the rate of recidivism and recurrence were evaluated. Recidivism was defined as patients with residual disease detected within 1 year of the initial procedure and recurrence was defined as new disease detected more than 1 year after definitive surgical intervention. A second look operation was performed for the CWU patients after 6 to 9 months to assess for recidivism.

Surgical Reconstruction Technique With Hydroxyapatite

The following surgical reconstruction technique using Stryker Hydroset hydroxyapatite was gathered after consultation with the operating surgeon on all cases presented in this study.

In the presence of a skull base defect, the tegmen is skeletonized to expose the defect. After achieving hemostasis, the ossicular chain is evaluated to assess if the height of the tegmen tympani and size of the defect, especially its medial extension, require disarticulation of the ossicular chain. If needed the incus is sharply disarticulated from the incudo-stapedial joint and cleared. The malleus head is then removed with a malleus nipper. An incus interposition is then performed through the facial recess. Neurosurgical cottonoids are placed over the horizontal segment of the facial nerve to prevent cement from entering the middle ear. In cases where it is determined that the chain can be left intact, the cottonoids are placed around the ossicular chain to prevent cement penetration onto the ossicular heads or into the middle ear. The hydroxyapatite cement is prepared following the manufacturer recommendations. With a dedicated syringe, the cement is layered gradually, starting at the epitympanum and progressively advancing laterally and posteriorly. With repeated applications, the hydroxyapatite cement is compressed with the use of neurosurgical cottonoids and suction before placing another layer. In this manner the whole tegmen, including the defect, is resurfaced with cement. No other materials such as fascia or cartilage are used. The repair is ideally completed in approximately 2 minutes. The cottonoids are used to compress and dry the cement concurrently. The cement is allowed to dry for 5 to 10 minutes and then the repair is inspected. For skull base defects, a Valsalva maneuver is completed to ensure that there is no CSF leak. The wound is observed for another 5 to 10 minutes during wound closure.

In case of a lateral semicircular canal dehiscence, a similar approach is employed. Any mucosal debris is cleared from the bony canal around the fistula. The matrix of the cholesteatoma is sharply dissected from the bony canal avoiding direct suction into the fistula itself. Hydroxyapatite cement is then layered over the fistula using a freer dissector, contouring the canal to its original shape, using gentle compression with neurosurgical cottonoids.

Statistical Analysis

Analyses were conducted using SPSS v.28. Nominal data were analyzed by means of χ^2 statistics or Fisher's exact probability test. A value of $P \leq .05$ was considered indicative of statistical significance. Continuous variables are represented with the mean and standard deviation.

Results

A total of 22 patients who underwent surgery for removal of cholesteatoma with repair of either tegmen defect or lateral semicircular canal fistula using hydroxyapatite cement were identified in a 10-year period. A total of 17 patients (77.3%) underwent a CWU tympanomastoidectomy followed by a second look operation to assess for recidivism. The remaining 5 patients (22.7%) necessitated a CWD tympanomastoidectomy approach due to the extent of the disease. In our cohort, 4 (18.2%) of the surgeries (all CWUs) were diagnosed with recidivism of the disease and the overall cholesteatoma recurrence rate was 4.5%. The demographic and surgical characteristics of both cohorts are presented in **Table 1**. The recurrence rate of a CSF leak was 4.5% (n = 1). Three (13.5%) patients had a local skin infection, not involving the hydroxyapatite cement, and 1 (4.5%) had a subacute complication due to a postoperative mastoid abscess. Importantly, there was no evidence of active infection at the time of surgery, per operative note report.

Infection Details

Two out of the 3 patients with local infections had very mild cellulitis and responded to conservative treatment. The exact time course regarding their infections was not documented per our chart review as follow-up was not needed. For the third patient, a small area of suture dehiscence was noted on postoperative day 6 and was treated with local antibiotics. The exact timeline for medical management was unclear, but all treatment was completed prior to the patient's postoperative appointment. The only patient with an infection in the mastoid cavity as identified during the second look operation. After the patient's initial surgery, they were discharged

Table 1. Demographics Table

| Factor (n = 22) | Mean ± SD | n (%) |
|---------------------------------|------------|-----------|
| Demographics | | |
| Age, y | 31 ± 12.6 | |
| BMI | 21.2 ± 8.8 | |
| Sex (M) | | 11 (50) |
| Smoking (never) | | 17 (77.3) |
| Race (white) | | 17 (77.3) |
| Surgical characteristics | | |
| Side of ear surgery (right) | | 7 (31.8) |
| Surgical technique | | |
| Canal wall up | | 17 (77.3) |
| Canal wall down | | 5 (22.7) |
| Recidivism rate | | 4 (18.2) |
| Recurrence rate | | 1 (4.5) |
| Recurrent leak | | 1 (4.5) |
| Local infection | | 3 (13.6) |
| Subacute infection | | 1 (4.5) |

Abbreviations: BMI, body mass index; M, male.

on 7 days of levofloxacin. On follow-up, no clinical concern of infection was raised. The patient was scheduled for a second look operation after 6 months for surveillance of recidivism. During the patient's second-look procedure, an intraoperative mastoid abscess was noted. They were admitted for postoperative IV antibiotics (Zosyn). After 2 days of treatment, they were discharged on levofloxacin for 10 days. No evidence of further complications was noted during the postoperative course of the second look.

Recurrence and Recidivism

We also found that in CWU surgeries, the recidivism rate is 23.5% and recurrence rate is 0% compared to 0% and 20% (n = 1/5), respectively, in CWD surgeries ($P = .54$, $P = .23$, respectively). Assessing differences by surgical ear laterality did not reach statistically or clinical significance.

In order to assess if the use of hydroxyapatite cement increases the risk of recidivism or recurrence, the results of matched control cases with cholesteatoma-induced skull base defect without the use of hydroxyapatite were identified. A control cohort of 22 patients throughout 2013 to 2022 controlled for gender, surgical approach, and surgical ear was identified. The overall recidivism rate was 18.2% (n = 4), and the recurrence rate was 4.5% (n = 1), which was identical to the cohort in which hydroxyapatite cement was utilized. In the control group, similar to the experimental, ear laterality did not reach statistical or clinical significance. When comparing the rates of recidivism and recurrence between the 2 groups there were no statistically significant differences seen. For patients with CWU surgeries, the rate of recurrence and recidivism were identical between the group with hydroxyapatite cement use and without (0% and 23.5%, respectively; $P = 1$ for both). For patients with CWD surgeries, the rate of recidivism was identical for both groups at 0% ($P = 1$) and the rate of recurrence was 0% for the control group and 20% (n = 1) for the hydroxyapatite cement group ($P = 1$).

There was 1 patient who had a true recurrence due to retraction pocket within the CWD cohort. This patient was initially successfully treated with CWD in 2013 for her cholesteatoma and was found to have a recurrence almost a decade later in Winter of 2022 in which she presented with an epitympanic retraction pocket in the CWD cavity. She was the single patient with a recurrence in our cohort.

Labyrinthine Fistulas

In the cohort of cholesteatoma-induced skull base defects, a subgroup of patients with a lateral semicircular canal fistula, which was largely identified intraoperatively, was analyzed further. To assess successful repair of cholesteatoma-induced lateral semicircular canal fistulas using hydroxyapatite cement in these patients the audiologic results were evaluated. All patients had stable bone lines on postoperative audiograms, with no worsening

sensorineural hearing loss. The improvement in air-bone gap (ABG) between pre- and postoperative audiograms was evaluated. Patients experienced an average of 37.8% improvement in ABG closure at 500 Hz, 24.3% at 1000 Hz, and 31.5% at 2000 Hz. Ossicular chain reconstruction was not conducted in these cases. We did not identify any patients with profound hearing loss either pre- or postoperatively in our cohort.

The average follow-up time for the study cohort was 3.0 ± 2.6 years and the average follow-up time for the control group was 2.5 ± 2.2 years with a minimum follow-up time of 1.5 years.

Discussion

Cholesteatoma is a surgically challenging disease with known high rates of disease recidivism. Many clinical and research efforts have been allocated in attempt to develop optimized surgical approaches to treat the disease effectively with the best anatomical and functional results without hampering the rate of residual disease.^{11,12} The results of this study are the first to demonstrate that implementing hydroxyapatite for repair of tegmen and labyrinthine defects due to cholesteatoma is effective and does not increase the risk of recurrence. Within our institutional cohort, our findings demonstrated that when using this synthetic material in cholesteatoma surgery, the overall recidivism and recurrence rates do not exceed those of the surgeries that didn't utilize hydroxyapatite. Additionally, in patients for whom the hydroxyapatite was used for semicircular canal repair following cholesteatoma removal, patients did not have any worsening sensorineural hearing loss and had improvement in conductive hearing loss. Hydroxyapatite could be considered an option in patients with larger defects or in those who do not have readily available autologous materials, such as in revision surgeries, given that hydroxyapatite is a more accessible robust alternative that can be utilized.

Cholesteatoma is locally aggressive and invasive, and this can lead to apprehension about introducing a synthetic material that can lead to complications or be a locus of recurrence. A meta-analysis investigating cholesteatoma recurrence rates by surgical technique, indicated that CWU approaches have a recurrence rate ranging from 9% to 70% with an average of 29.6% and CWD approaches, regarded as a definitive treatment for cholesteatoma, can have a recurrence rate of 5% to 17% with an average of 8.6%.¹³ Our control cohort had a similar average rate of recurrence to that noted in the current literature, when combining the recidivism and recurrences of our cohort. Additionally, since the hydroxyapatite group within our study did not have comparatively different rates of either recidivism or recurrence compared to the control group, our findings support the idea that the use of cement for repair may not place patients at an increased risk for disease recurrence.

In our cohort, patients who underwent CWU with hydroxyapatite had higher recidivism rates while those with CWD had higher rates of recurrence; however, these differences didn't reach clinical significance, most probably due to our cohort size. In CWD surgeries, the posterior external ear canal wall is progressively removed and lowered to the facial ridge, either to allow improved access and exposure of the disease or due to extensive erosion of key structures. This technique has been reported to reduce the rates of recidivism.¹⁴ Thus, the greater rates of surgical success seen in CWD cohorts with or without hydroxyapatite cement and the higher recidivism rates in CW approaches are in line with current literature and in consensus that CWD is a more definitive surgery to address cholesteatoma. The use of hydroxyapatite was not found to increase either the risk of recidivism in CWU or recurrence in the CWD cohort. Moreover, the use of the hydroxyapatite in the setting of CWD was not found to increase the risk of infection despite using a synthetic material in an open cavity.

The use of hydroxyapatite for the repair of lateral semicircular canal dehiscence due to cholesteatoma has also been shown to be safe with favorable hearing results in our study. It could afford the ability of removing the cholesteatoma matrix and repairing the fistula without necessitating a CWD approach due to the dehiscence.

When discussing cholesteatomas, there is a potential concern of introducing a foreign body in a possibly contaminated cavity. This is especially of concern while repairing the skull base or labyrinthine fistula. Our results demonstrate an overall low risk of infection (1 patient with a mastoid abscess) as well as 3 local wound infections, which were treated successfully expectantly with no surgical intervention needed. A meta-analysis reviewing previous experience with hydroxyapatite in middle ear surgeries reported an infection rate of 1% to 6%, similar to our results.¹⁵ It is possible that the inflammatory nature of cholesteatomas could have contributed to the slightly higher rate of local infections seen in our cohort. However, these were managed conservatively with minimal or no postoperative antibiotic care. There was 1 patient who experienced a mastoid abscess, but the patient was treated with antibiotics and managed expectantly. Further studies are needed with a larger sample size to assess the generalizability of this nature of infection.

In the setting of cholesteatoma eroding the skull base with resultant CSF leak, we would expect a lower recurrence rate of the leak when compared to spontaneous CSF leaks in which the presumed cause is increased intracranial pressure. Our study demonstrates that hydroxyapatite allows for a high rate of successful repair that is durable with only 1 recurrent CSF leak. Previous literature exploring repairs of CSF leaks with hydroxyapatite have reported recurrence rate of 0% to 3.4%, on par with what was seen in our study.^{4,16} Thus, even in the setting of cholesteatoma with possible concurrent biofilm

or infection, the hydroxyapatite remains durable affording a reliable option for repair of skull base.

Despite being the first study to investigate the use of hydroxyapatite in the setting of cholesteatoma disease, this study has limitations which include its small sample size and the retrospective nature of investigation. Given that our cohorts were 22 patients each, analysis of the different surgical techniques was unable to demonstrate statistical significance within the hydroxyapatite group and between the 2 groups due to lack of power. Additionally, while we were able to compare our cohort of interest against a control cohort by standardizing gender and surgical technique, we were unable to control for comorbidities, which may have a bearing on surgical outcomes. Additionally, controlling for procedure still does not entirely control for the severity or extent of disease. Future multicenter prospective studies will allow better understanding of the optimized patients and disease process in which hydroxyapatite cement can be used safely and efficiently. Longer follow-up studies are warranted to ascertain the durability of these repairs and any possible increased risk for infections or local complications long term.

While quicker operating time has been cited as an advantage of hydroxyapatite use in literature, we were unable to assess this aspect in relation to cholesteatoma removal. Since these surgeries can often be inherently lengthy due to the unpredictable nature of cholesteatoma disease spread, we were unable to isolate the length of surgery attributed to hydroxyapatite use in the operative time. Future prospective studies could conduct a cohort-control trial to assess specifically this quality of hydroxyapatite in cholesteatoma removal procedures.

Conclusion

Within our cohort, we demonstrated that the use of hydroxyapatite cement to repair skull base defects and labyrinthine fistulas can serve as an effective technique which does not incur a higher rate of cholesteatoma recurrence or recidivism. Hydroxyapatite cement is a readily available and highly malleable material, which may prove to be a viable alternative option for improved patient outcomes and quality of care. Additional studies are needed to reach firm conclusions that can be generalized to the public.

Author Contributions


Rema Shah, study conception and design, data collection and analysis, manuscript writing and editing; **Allison Reeder**, data collection and analysis, manuscript editing; **Sarah G. Wilkins**, data collection and analysis, manuscript editing; **John Kveton**, study design, data analysis, manuscript editing; **Nofrat Schwartz**, study conception and design, data analysis, manuscript editing.


Disclosures

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