Advantages of Hyaluronic Acid Fat Graft Myringoplasty Over Fat Graft Myringoplasty

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**Objectives:** To compare hyaluronic acid fat graft myringoplasty (HAFGM) with fat graft myringoplasty (FGM) on grade 1 tympanic membrane perforations (TMPs) (<25% of the tympanic membrane surface) and to assess 12-month postoperative hearing outcomes in a pediatric population.

**Design:** Prospective study.

**Setting:** Tertiary care pediatric center.

**Patients:** Ninety-two children with a TMP were included in the study and were operated on using either the HAFGM (n=50) or FGM (n=42) technique. Age at surgery ranged from 4 to 17 years (mean age, 11.52 years).

**Interventions:** Hyaluronic acid fat graft myringoplasty is a new technique for TMP repair in a pediatric population and is performed using local anesthesia at the outpatient office.

**Main Outcome Measures:** Postoperative status of the tympanic membrane, hearing improvement, and incidence of complications.

**Results:** Successful closure of the tympanic membrane was achieved in 90% of the HAFGM group and in 57.1% of the FGM group (P<.004). The mean (SD) postoperative air-bone gap in the HAFGM (6.86 [8.52] dB) group was significantly lower than in the FGM (18.32 [13.44] dB) group (P<.002). The mean postoperative follow-up time was 31.5 and 34.7 months for HAFGM and FGM groups, respectively. No difference was observed between children 10 years or younger and children older than 10 years. In the 2 groups, no postoperative complications were observed. The location of the perforation was not found to be a factor indicative of failure.

**Conclusions:** The success rate of HAFGM is superior to that of FGM alone. Hyaluronic acid fat graft myringoplasty can be performed as an office-based procedure using local anesthesia and requires no hospitalization. Because of its substantial advantages, HAFGM could be considered as the first choice for the reconstruction of a dry TMP in the pediatric population.


**Tympanic Membrane Perforation (TMP) commonly results from infection or trauma or is the sequela of tympanostomy tube insertion. Although 88% of traumatic TMPs of all sizes will heal without intervention, the remaining 12% can become chronic and require treatment. Persistent TMP is a commonly encountered condition in a general ear, nose, and throat practice. A persistent TMP increases the patient’s risk of developing recurrent acute otitis media or chronic middle ear disease, conditions that are frequently associated with an unpleasant otorhea. When a TMP is present, the damaged tympanic membrane becomes acoustically inefficient, and this can lead to conductive hearing loss. Myringoplasty without elevating the annulus and entering the middle ear is a commonly performed procedure in the pediatric population. Although, a large variety of techniques have been described in the literature, it is difficult to determine which technique is best suited for the repair of a TMP in the pediatric population.

In 1962, Ringenberg was the first to describe fat plug myringoplasty and reported a success rate of 87% for small perforations. Since then, studies have reported success rates ranging from 76% to 92% in cases of small TMPs. Deddens et al found TMP size to be a crucial factor in predicting success for tympanoplasty. In their series, perforations of 5% to 30% of the tympanic membrane surface were found to be a good prognostic factor for the success of fat graft myringoplasty (FGM), whereas larger perforations were more prone to failure.

In 2008, Saliba described the hyaluronic acid fat graft myringoplasty (HAFGM) and reported, after an 18 months follow-up, a global success rate of 92.7% in adults and 87% in children for all TMP sizes combined. The HAFGM technique did not require hospitalization for pediatric patients and had the advantage of being feasible in children using lo-
otal anesthesia. The success rate of HAFGM was found to be comparable to the success rates of underlay and overlay techniques. Moreover, a recent study evaluating the efficacy of hyaluronic acid ester films alone for TMP repair by Prior et al.\textsuperscript{10} had to be abandoned because the preliminary results failed to show any sign of successful closure of the TMP.

The present study was designed to compare the success rates of HAFGM with FGM techniques for grade 1 TMPs (<25% of the tympanic membrane surface) in a pediatric population and to assess the 12-month postoperative hearing outcomes.

**METHODS**

**PATIENTS**

This study was conducted prospectively from 2008 to 2010 at our tertiary care pediatric center. All patients were children younger than 18 years, who were operated on using local anesthesia at the outpatient clinic. Under microscopic vision, tympanic membrane was virtually divided into 4 quadrants: the posteroinferior, anterosuperior, and anteroinferior quadrants. The aim of dividing the tympanic membrane into quadrants was to facilitate the measurement of size and location of the TMP. The size of the perforation was estimated as a percentage and was graded according to TMP classification of Saliba, reported in 2008.\textsuperscript{7,11}

All children satisfying the following criteria were included in the study: (1) grade 1 TMP, (2) perforation present for at least 6 months, (3) no evidence of otorrhea or active chronic otitis media, cholesteatoma, or retraction pocket formation, (4) no suspected ossicular pathology on microscopic examination, and (5) preoperative air-bone gap (ABG) of 35 dB or better. The following exclusion criteria were used: (1) patients in whom the anterior rim of the perforation was not identifiable or was hidden by the anterior wall bulge of the external auditory canal in order to avoid a blind surgical procedure and (2) perforation of grade II or more. Because most authors seem to agree on a maximal perforation size of 30% of the tympanic membrane surface to perform a FGM, we reserved our indications for perforations of grade I. All patients and parents received a full description of the procedure (ie, surgical technique, risks, complications, advantages) and signed an informed consent form.

**HAFGM AND FGM SURGICAL TECHNIQUES**

A complete description of the FGM\textsuperscript{12,13} and of the HAFGM\textsuperscript{7,9} techniques can be found elsewhere and will not be detailed in this article. However in both techniques, the lateral fat graft bulge should not be placed too high. The fat graft is harvested through a 5-mm cutaneous incision below the mastoid tip and behind the sternocleidomastoid muscle near the midline. The only difference between the FGM and the HAFGM techniques is that in the HAFGM technique, the fat graft and the tympanic membrane remnant are covered by a hyaluronic acid EpiDisc (Medtronic Xomed). Care should be taken to get an intimate contact between the EpiDisc, the fat graft and the intact epithelium edge of the perforation. The EpiDisc is an 8-mm-diameter transparent otologic lamina of hyaluronic acid ester. It has microperforations that allow permeability and exudative drainage at the surgical site.

**OUTCOME MEASURES**

The following data were recorded for every patient: sex, age, preoperative otologic symptoms, primary or revision surgery, perforation location and side. The postoperative status of the tympanic membrane, the improvement of hearing and the incidence of complications were used to measure outcomes. The mean values of the preoperative and postoperative air conduction and bone conduction thresholds at the frequencies 500, 1000, 2000, and 4000 Hz were used to compute pure-tone average and ABG closure. A postoperative bone conduction threshold increase of 10 dB or more or a 20% decrease in the speech discrimination score was considered as a significant sensorineural hearing loss. Follow-up was scheduled at 2, 4, and 12 months after the procedure and then on a yearly basis. Successful closure of the tympanic membrane and graft failure rates were based on the status of the tympanic membrane at the most recent visit, at minimum of 12 months postoperatively. Hearing improvement was assessed using audiogram results obtained at 4 and 12 months postoperatively.

**STATISTICAL ANALYSIS**

Statistical analysis was performed using variance analysis with repeated measures and the $\chi^2$ test. $P<.05$ was considered statistically significant.

**RESULTS**

This study population comprised 92 patients. In the HAFGM group (n=50), age at surgery ranged between 4 and 17 years, with a mean (SD) of 11.68 (3.53) years. The male to female ratio was 1.51:1, and 55% of patients were operated on the right and 45% on the left side.

In the FGM group (n=42), age at surgery ranged between 5 and 16 years, with a mean (SD) of 11.26 (3.21) years. The male to female ratio was 1.13:1, and 41% of patients were operated on the right and 60% on the left side.

Age, sex, and side of TMP were not found to be statistically different among the 2 groups ($P=.59$, $P=.08$, and $P=.06$, respectively). By assessing age as a categorical variable (10 years or younger and older than 10 years), no significant difference in success rates was found between the 2 age categories in each group. However, the difference in success rates was significant between the FGM and HAFGM groups in each age category (Table 1). Preoperative symptoms, history of a otologic surgery in the operated ear, and location of TMP are summarized in Table 2. For all theses evaluated factors, no difference be-

**Table 1. Myringoplasty Results When Age Was Assessed as a Categorical Variable**

<table>
<thead>
<tr>
<th>Age, y</th>
<th>HAFGM Group, No. (n = 50)</th>
<th>FGM Group, No. (n = 42)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤10</td>
<td>Success 14</td>
<td>9</td>
<td>.01</td>
</tr>
<tr>
<td></td>
<td>Failure 2</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>&gt;10–18</td>
<td>Success 31</td>
<td>15</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Failure 3</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>NA</td>
<td>.37</td>
<td>.59</td>
</tr>
</tbody>
</table>

Abbreviations: FGM, fat graft myringoplasty; HAFGM, hyaluronic acid fat graft myringoplasty; NA, not applicable.
warrant the 2 postoperative audiograms in each group. No worsening of bone conduction threshold was noted postoperatively in the 2 groups. Therefore, HAFGM, along with the conventional FGM, are both safe techniques.

No difference was noted between the preoperative mean (SD) ABG of HAFGM (19.95 [12.78] dB) and FGM (15.88 [9.06] dB) groups (P = .03). However, the postoperative mean (SD) ABG of the HAFGM group (6.86 [8.52] dB) was significantly better than the ABG of the FGM group (18.32 [13.44] dB) (P = .002). Air-bone gap improvement was found to be clinically and statistically significant only in the HAFGM group (P = .002) (Figure 1). When we compared the hearing results after discarding the failure cases of both groups, no significant difference was identified in the postoperative hearing results (P = .37). Preoperative and postoperative pure-tone average, bone conduction threshold, and speech discrimination score are detailed in the Table 4. The mean hearing improvement for the operated ear was 10.75 dB for the HAFGM group and 4.75 dB for the FGM group.

The mean duration of the operative procedure was 16 minutes for the HAFGM group and 15.2 minutes for the FGM group. A statistically significant difference was identified in the postoperative hearing results (P = .004). All cases of failure occurred in the first 4 months postoperatively in both groups (P = .90). In both groups, location of the perforation was not found to be a factor indicative of failure. Detailed results are presented in Table 3.

Hearing was assessed preoperatively and postoperatively at 4 and 12 months. No difference was found between the 2 postoperative audiograms in each group. No worsening of bone conduction threshold was noted postoperatively in the 2 groups. Therefore, HAFGM, along with the conventional FGM, are both safe techniques.

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The mean duration of the operative procedure was 16 minutes for the HAFGM group and 15.2 minutes for the
FGM group ($P = .54$). The mean postoperative follow-up was 31.5 and 34.7 months for the HAFGM and FGM groups, respectively ($P = .12$). At 12 months postoperatively, we found a small remnant of fat graft in the tympanic membrane thickness of all successful cases of HAFGM and in some successful cases of FGM. No causes of failure were identified, with the exception of 1 case of infection in the HAFGM group (2%). We noted the absence of complications, such as cholesteatoma development, tympanic membrane lateralization, blunting, or retraction pocket formation.

**COMMENT**

The closure of TMPs with a fat graft is a well-known and commonly performed procedure in the pediatric population. However, this technique is limited by its low success rates, as well as by the size of the TMP. Therefore, FGM is performed in small TMPs.5,6,13

Hyaluronic acid is a naturally occurring extracellular polysaccharide. It is a component of the extracellular matrix of many bodily tissues, making it highly biocompatible. The effects of hyaluronic acid are believed to be related to the regulation of the healing pattern of the fibrous layer and prevention of dehydration of the perforation margins.1,15 Two additional proposed effects are to provide a supportive media for the excess keratin and hyperplastic epithelium, which typically occurs during the healing process, and to regulate cell functions by increasing the motility and phagocytic functions of the polymorphonuclear leukocytes.16,17

The fat graft plays a role of support and presents an important revascularization activity. This phenomenon can be observed by otoscopy at 2 months postoperatively (Figure 2). Studies performed on the vascularization of fatty tissue showed that angiogenesis precedes adipogenesis. Moreover, the adipose tissue promotes cicatrization and revascularization of nonvascularized areas.18,19 These properties are intimately related to the secretory activity of adipose cells, which produce numerous proinflammatory and proangiogenic proteins and metabolites.20 Furthermore, epithelial cell migration is stimulated by hyaluronic acid. Hyaluronic acid allows a complete epithelial cell migration before the resorption of the fat plug. Hyaluronic acid EpiDisc stimulates a centripetal migration of the epithelial layer over the temporary fat graft support. This is why an intimate contact, with no excess pressure, between the hyaluronic acid EpiDisc and the intact epithelial edge around the perforation is necessary. In contrast to the described “champagne cork” technique of fat insertion into its half,13 we recommend a complete insertion of the fat graft in the middle ear, leaving a very thin lateral bulge through the perforation that approximates the level of the tympanic membrane remnant. This technique of fat insertion allows for a more direct epithelial cell migration over the fat graft with a shorter time for the migrated cells to meet together.

Repair of TMP with hyaluronic acid ester films alone is not recommended. One study showed that the sheet of hyaluronic acid, trimmed to a size roughly 2 mm larger in diameter than the perforation and tucked through the perforation, dissolved with no epithelial cell migration, while the perforation size remained the same.10

Because the success rates of the FGM technique are very low, even in the presence of small perforations (grade I), the HAFGM technique proved to be superior to FGM technique. Moreover, HAFGM had already proven to be equivalent to the overlay and underlay techniques in both the pediatric and adult population. The HAFGM technique allows for a high success rate for perforations of all sizes and in all quadrants if a complete visualization of the epithelial margin is possible.8,9 With HAFGM, there is no need for general anesthesia, and the procedure can be performed in the outpatient clinic. For some patients, the risks, costs, and inconvenience of an operation are significant concerns. These patients may benefit from a simple, inexpensive, and outpatient alternative that allows patients to continue their activities on the same day as the surgery.

The success rates for repair of our grade I perforations was 90% using the HAFGM technique and 37%
using the FGM technique. These results confirm the superiority of the HAFGM technique over the FGM technique and reflect the importance of the hyaluronic acid EpiDisc in the tympanic membrane healing process. Published rates of success for FGM have been as high as 85% for small perforations.8-11 Since the term small perforation was not well defined in the previous studies, we cannot compare our low success rate of FGM to the high success rate reported in the literature.

All of our failure cases were identified in the first 4 postoperative months in both groups. Jurovitzki and Sade22 showed that TMPs recurred over the years to a degree that turned an initial success into a failure in 7.6% of patients who underwent traditional myringoplasty.

In our study, patients were followed up to 35 months, and no recurrences were observed after the fourth postoperative month. These results illustrate the stability and the high quality of the newly developed tympanic membrane. Histological properties of FGM have been investigated in guinea pigs and cats, showing a normal appearing outer epithelium and middle ear mucosa.22-24 The fat graft progressively disappears, leaving in place a thin sheath of fat between the new mucosa and the epithelial tissue. This remaining fat is the signature of the HAFGM technique and persisted in our study until the most recent follow-up examination (Figure 3). Unlike previously reported data by Ozgursoy and Yorulmaz,25 our postoperative otoscopic examinations did not identify a sclerotic area on the TM. We believe that hyaluronic acid may play a role in fat graft remodeling.

Postoperative hearing test results as well as the improvement in the ABG at 1 year were similar to those obtained at 4 months. These results depict the stability in the hearing improvement and serves as evidence that a small fatty thickness in the eardrum does not affect hearing results. Sensorineural hearing loss is a very rare complication of tympanoplasty. To date, sensorineural hearing loss has not been reported in any study evaluating fat graft myringoplasty, including our study.5,6,8,9,14 We found that among the cases of FGM failure, 22% developed larger perforations after surgery (grade II). This increase in perforation size may explain the postoperative nonsignificant worsening of the ABG in this group.

Age at which myringoplasty should be performed remains a debated topic in the literature. Children have an increased predisposition for middle ear disease and are more susceptible to upper respiratory tract infections and eustachian tube dysfunction. Many physicians are opposed to performing myringoplasty on young children and prefer postponing the surgery to a later date. We assessed age as a categorical variable and found that age was not to be a factor predictive of success, regardless of the technique used. However, the number of patients in each age category was too small to achieve significant statistical power. Careful attention to the eustachian tube function will likely increase the rate of an intact tympanic membrane with improvement in hearing, but age in itself should not be an indication for or against treatment.26,27

In conclusion, the success rate of HAFGM is superior to that of FGM alone. Hyaluronic acid fat graft myringoplasty can be performed as an office-based procedure with local anesthesia and requires no hospitalization. The postoperative ABG improvement reflects the excellent repair of the tympanic membrane and serves as evidence for the quality of the new tympanic membrane and hearing restoration. Because of its substantial advantages, HAFGM could be considered as the first choice for the reconstruction of a dry TMP in the pediatric population.

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Author Contributions: Dr Saliba had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Saliba, Knapik, and Froehlich. Acquisition of data: Saliba and Knapik. Analysis and interpretation of data: Saliba and Abela. Drafting of the manuscript: Saliba. Critical revision of the manuscript for important intellectual content: Saliba, Knapik, Froehlich, and Abela. Statistical analysis: Saliba. Administrative, technical, and material support: Saliba and Knapik. Study supervision: Saliba, Froehlich, and Abela.

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REFERENCES


