Statistical Evaluation of 231 Ears That Received Tympanic Membrane Perforation Closure Using Carbon Dioxide Laser and Collagen Sponge

Kazuhiro Kuroda[1] Tatsuaki Kuroda[1]

[1] Kuroda Otorhinolaryngology Clinic, Yatsusiro-shi, Kumamoto, Japan

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Address for correspondence Kazuhiro Kuroda, MD, Kuroda Otorhinolaryngology Clinic, 1513-1 Kagami-machi, Yatsushiro-shi, Kumamoto 869-4215, Japan (e-mail: kazu@kuroda33.com).

Abstract

The tympanoplasty technique reported by Yuasa et al, wherein autologous tissue is fixed to the perforated tympanic membrane using fibrin glue, is widely used. This technique has also led to the development of several simpler surgical methods using artificial materials not involving the use of fibrin glue. We used a carbon dioxide laser device (OtoLAM, Lumenis Be Japan Inc.) during tympanoplasty to refresh the perforation margin of the tympanic membrane and a collagen sponge with a silicone membrane (Terudermis, Alcare Inc.) as the closure material for tympanoplasty. OtoLAM is used to refresh the perforation margin in a short time. By simply fixing Terudermis to the perforated area using the attached silicone membrane, the surgery can be performed in a short time without the need for autologous tissue collection. For the past 9 years and 5 months, from June 2013 to November 2022, we used this method for tympanic membrane perforation closure in 231 ears. The closure rate after a single operation was not high (78/231; 33.8%) but significantly improved with multiple attempts (161/231; 69.7%). The advantages of this technique are that it is simple, can be performed quickly, is economical as it does not involve the use of fibrin glue, and there is no possibility of blood infection, eliminating the need for a detailed explanation to the patient.

Keywords
- tympanoplasty
- OtoLAM
- Terudermis

Introduction

Various techniques for tympanic membrane perforation closure via the external auditory canal have recently been attempted. These have been conducted to replace the traditional myringoplasty technique that is performed via a pre- or postauricular incision. The adhesive-based myringoplasty technique reported by Yuasa et al,[1] wherein autologous tissue collected from a posterior auricular area is fixed to the perforated tympanic membrane using fibrin glue, is widely used. In addition to this technique, several simpler methods have been developed that use artificial materials instead of autologous tissue and do not use fibrin glue. These methods reported to date include those using a chitin membrane (Beschitin, Nipro Corporation, Osaka, Japan), a collagen sponge (Terudermis, Alcare Inc. Tokyo, Japan), and a basic fibroblast growth factor–impregnated gelatin sponge (Retympa, Novel Pharma, Co., Ltd., Tokyo, Japan). All these have demonstrated high closure rates.

At our hospital, tympanic membrane perforation closure is performed using a carbon dioxide laser tympanostomy device to refresh the tympanic membrane perforation margin and a bilayer collagen sponge with a silicone membrane

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as the closure material. This study aimed to conduct a statistical evaluation of 231 ears that underwent tympanic membrane perforation closure at our hospital from June 2013 to November 2022. All cases were observed for ≥2 months to evaluate the successful closure rates after single and multiple surgeries and assess the causes of failure.

Materials and Methods

Patients

We performed tympanic membrane perforation closure on 244 ears (in 222 patients) over a period of 9 years and 5 months, from June 2013 to the end of November 2022. Patients with no hearing improvements in patch tests, large perforations with only the circumference of the tympanic ring remaining (notably, we used the same procedure for large perforations of up to three quadrants if the perforation margin was clearly visible), invisible perforation margin due to curved or narrow external auditory canal, absent posterosuperior perforation margin, and suspected otitis media related to pars tensa cholesteatoma were excluded. Patients with otorrhea at the initial visit first underwent treatment with ear solutions or other drugs; surgery was performed only after they no longer had ear discharge from the tympanic cavity. For 242 ears, the follow-up period was ≥2 months. Success or failure of closure was evaluated in 231 ears (210 patients). We also evaluated the distribution of sex and age and the association of closure rates with age, perforation size, and cause of perforation.

Methods

The surgical procedure is illustrated in ►**Fig. 1**. A piece of cotton soaked in a T-CAIN anesthetic solution (T-CAIN, 20 g; phenol, 20 g; glycerin, 40 g; and menthol, 20 g in 100 g) was placed on the perforation to anesthetize the tympanic membrane (►**Fig. 1A**). After 10 minutes, a piece of cotton soaked in Tarivid otic solution was inserted into the perforation to protect the tympanic cavity from laser irradiation. The perforation margin of the tympanic membrane was then refreshed by irradiation using a carbon dioxide laser tympanostomy device (0.6–0.8-mm diameter; 10–15 W; OtoLAM, *Lumenis Be Japan Inc., Tokyo, Japan*) several times (►**Fig. 1B**). Thereafter, the size of the collagen sponge with silicone membrane (Terudermis) was adjusted such that it was slightly larger than the perforation size, and the silicone membrane was trimmed to an even larger size so that the whole membrane does not fall into the perforation. The resulting Terudermis with silicone membrane was adjusted such that it fitted within the perforation, which concludes the surgery (►**Fig. 1B, C**). The surgical duration was 15 to 20 minutes, including time for anesthesia.

The perforation margin was refreshed by irradiation using OtoLAM at 10 to 15 W in the narrowest possible width. Notably, the tympanic membrane perforation rarely increased in size after the treatment. Narrower irradiation ranges should be used for the perforation margins of thin tympanic membranes without inflammation. OtoLAM has a monitor for observation and can be used to perform accurate and rapid margin refreshment.

The patients were instructed to refrain from behaviors that could result in dislocation of the Terudermis, such as strong nose-blowing, pressing the ear with the palm, and insertion of a fingertip into the external auditory canal. Follow-up at the clinic was scheduled every 2 weeks. An uneventful postoperative course led to complete closure of the tympanic membrane perforation within approximately 2 months after surgery. The patients were informed in advance that this procedure is repeated up to three times as a general rule in case perforation closure is not achieved after the initial surgery and that the cumulative rate of successful closure is approximately 70% after three surgeries. The second and subsequent closure attempts are billed to insurers as patch tests (middle-ear function tests).

This study was approved by the Japan Medical Association Ethics Review Committee (R4–12). Prior to surgery, the patients and their family members were informed about other inpatient surgical treatment options, such as myringoplasty at a different institution, before taking their consent to perform the surgery.

Results

Of the 244 ears that underwent perforation closure during the study period of 9 years and 5 months, 231 ears (210 patients) were followed up for ≥2 months and perforation

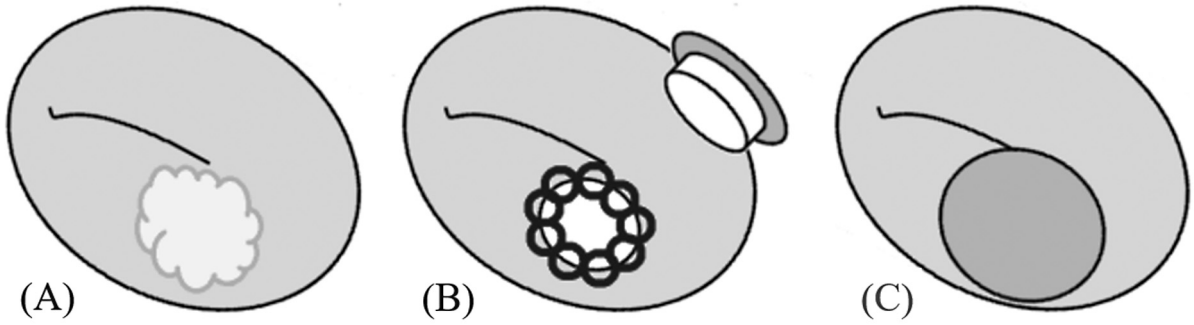


Fig. 1 Surgical procedure (left ear). (**A**) The perforation margin of the tympanic membrane is anesthetized using cotton soaked in a T-CAIN anesthetic solution. (**B**) The perforation margin of the tympanic membrane is refreshed with OtoLAM, and then the Terudermis with silicone membrane is trimmed. (**C**) The trimmed Terudermis with silicone membrane is fitted within the perforation.

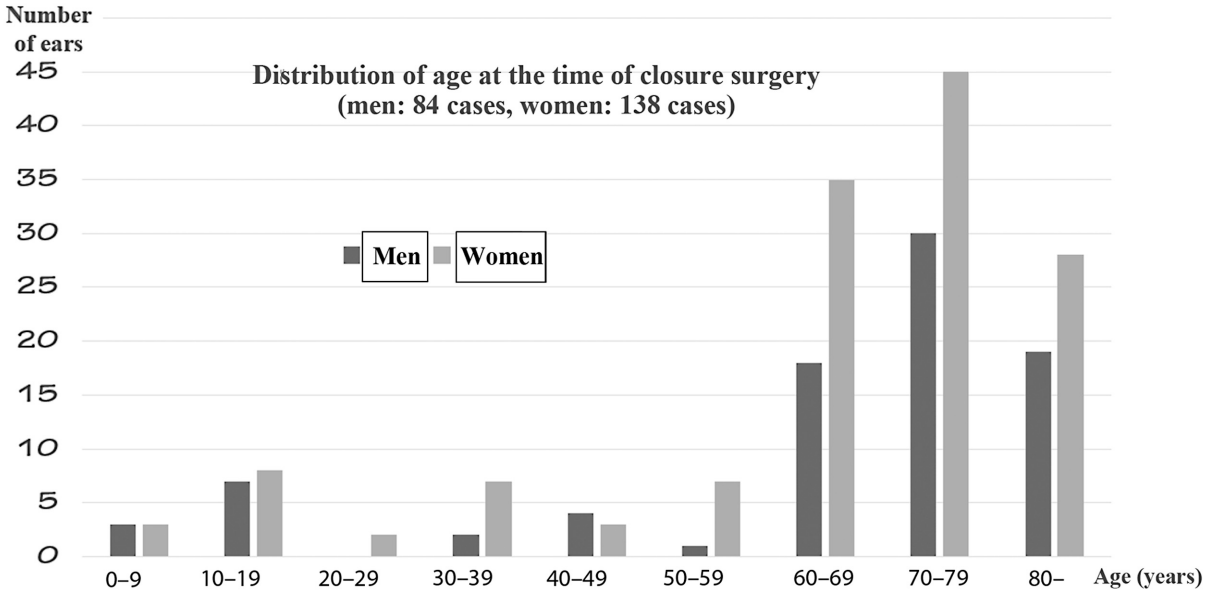


Fig. 2 Age distribution of men and women who underwent tympanic membrane perforation closure. Elderly patients tended to account for larger proportions among both men and women than the proportions of other age groups.

closure success was determined. The 210 patients included cases of 11 bilateral perforations and 10 reperforations between 4 months and 2 years after a successful closure.

►**Fig. 2** presents the age and sex distribution of the 222 patients. Elderly patients tended to account for larger proportions. ►**Fig. 3** presents the age distribution and closure rates for the 231 ears that were evaluated for closure success. Among the 68 ears without closure, the perforation size was reduced in 25 ears, including 7 ears in which perforation size was reduced to pinhole sizes. Some previous reports have considered perforations reaching pinhole size as successful closures; however, in this report, such cases were included as closure failure. There were no cases with postoperative increase in perforation size. Perforations were closed in 78 ears (33.8%) after a single operation and in 161 ears (69.7%) after multiple operations. The chi-squared test of closure rates in patients in different age groups revealed that the closure rate in patients aged ≥80 years was significantly higher at 82.2% (37/45; $p < 0.05$; ►**Fig. 3**).

►**Fig. 4** presents the relationship between closure rates and perforation sizes. Perforations limited to one quadrant were classified as small perforations, those up to two quadrants were classified as medium perforations, and those measuring three quadrants or larger were classified as large

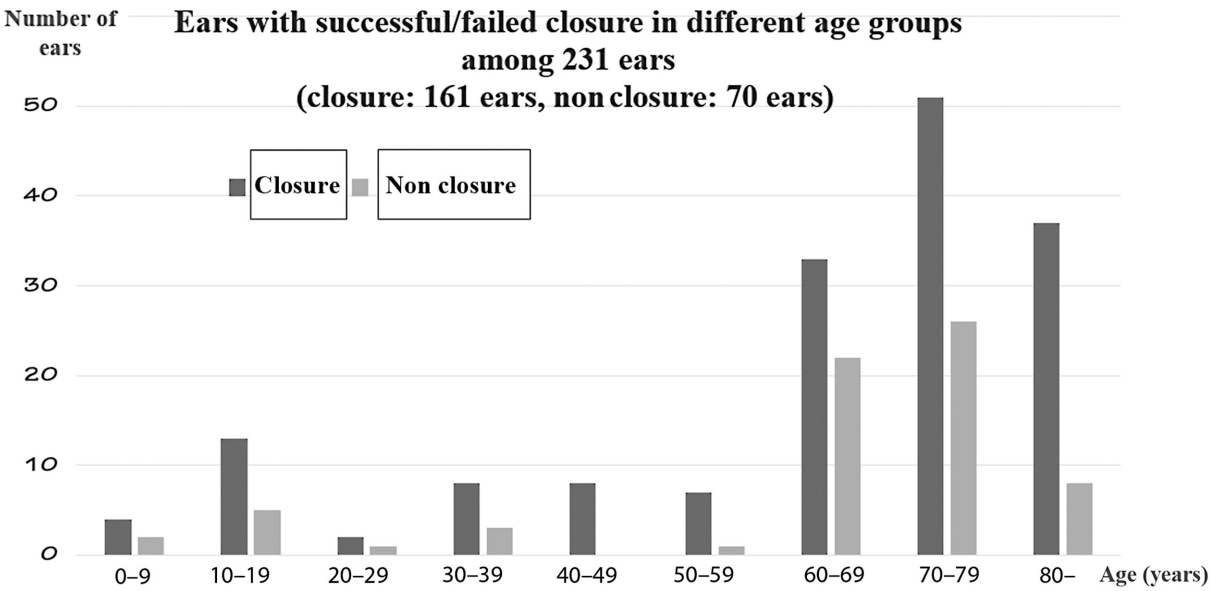
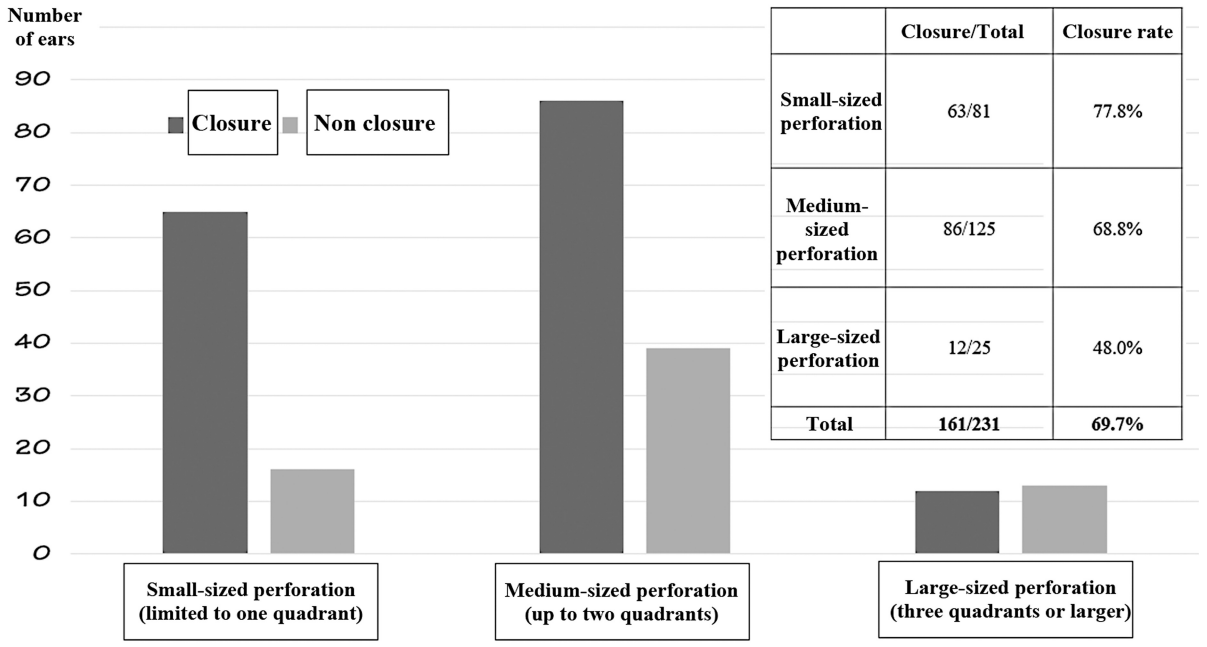


Fig. 3 Closure rates in different age groups among ears that underwent tympanic membrane perforation closure. The closure rate in patients aged ≥80 years was significantly higher at 82.2% (37/45) than that of younger patients.



	Closure/Total	Closure rate
Small-sized perforation	63/81	77.8%
Medium-sized perforation	86/125	68.8%
Large-sized perforation	12/25	48.0%
Total	161/231	69.7%

Fig. 4 Tympanic membrane perforation sizes and closure rates. The closure rate of small perforations was significantly higher and the closure rate of large perforations was significantly lower than the rates of the other respective sizes.

perforations. Although the overall closure rate was 69.7% (161/231), the closure rates for the small, medium, and large perforations were 77.8% (63/81), 68.8% (86/125), and 48% (12/25), respectively. The chi-squared test of these closure rates revealed that the rate of small perforations was higher ($p < 0.05$) and that of large perforations was lower ($p < 0.05$) than those of the other two respective sizes.

►**Table 1** presents the closure rates based on the causes of perforation. The following four causes of perforation were identified: traumatic, post-tympanostomy tube insertion, reperforations at 4 months to 2 years after initial closure, and other causes related to chronic otitis media. Perforation closure was performed ≥6 months after traumas in all of the traumatic cases except in one where closure was performed 3 months after the trauma because the perforation did not show a tendency toward closure within 3 months. The closure rates were not significantly different for the causes.

Table 1 Causes of perforation and closure rates

Cause of perforation	Ears with successful closure/total	Closure rate (%)
Trauma	11/13	84.6
After tympanostomy tube insertion	9/14	64.3
Reperforation after closure surgery	6/6	100
Other	135/198	68.2
Total	161/231	69.7

►**Table 2** presents the number of ears that achieved closure and the closure rates after the number of surgeries. The closure rate after a single operation was low at 33.8%; however, this rate cumulatively improved after each surgery, finally reaching 69.7%.

Representative Case

A representative case is shown in ►**Fig. 5**. The patient was a 58-year-old woman who experienced chronic otitis media since childhood. She had undergone myringoplasty as an inpatient 2 years ago, after which her perforated tympanic membrane did not close, and she visited us for closure as an outpatient. The tympanic membrane findings ≤1 year after surgery and mean hearing acuity are presented in ►**Fig. 5**. Closure was achieved after a single operation, and the mean hearing acuity improved from 33.75 to 16.25 dB.

Discussion

##Various tympanic membrane perforation–closure and myringoplasty procedures have been reported. They primarily differ in the following four aspects: how the perforation margin of the tympanic membrane is refreshed, the closure material used to close the tympanic membrane perforation, how the closure material is fixed, and whether an autologous serum or basic fibroblast growth factor are used for promoting tympanic membrane regeneration.

Treatment with 10% silver nitrate to refresh the perforation margin has been reported.[2,3] This is a simple method and requires no special skills, although the closure rate with autologous serum ear drops is not very high (61.8%; 24/55).[2] Another method that uses a needle or a similar tool to

Table 2 Number of operations required to achieve closure

No. of operations	Ears with successful closure/total	Closure rate (%)
1	78/231	33.8
2	47/231	20.3
3	23/231	10.0
4	5/231	2.2
≥5	8/231	3.5
Total	161/231	69.7

remove the circumference of the perforation margin as a band has been described in many reports. Adequate refreshing can be accomplished in this method, but it requires a certain level of experience and technique. Further, if perforation does not close, there is a possibility of perforation expansion. We used OtoLAM, a carbon dioxide laser device for tympanostomy, to refresh the perforation margin. OtoLAM is a computer-controlled, precision laser irradiation device that enables instant and accurate incisions of the tympanic membrane at the desired size and position with the help of a monitor for observation. Using the OtoLAM device, a desired area of the perforation margin of the tympanic membrane can be irradiated and refreshed quickly and accurately. Caution is needed to avoid damaging the chorda tympani nerve when an area posterosuperior to the residual tympanic membrane is irradiated. Currently, we use OtoLAM output values between 10 and 15 W; however, the perforation margin may not be refreshed sufficiently if inflammation thickens the tympanic membrane. In the future, we plan to use higher output values to assess the improvement in closure rate.

In myringoplasty, autologous tissues, such as fasciae and connective tissue, have been used as perforation closure materials. The adhesive-based method reported by Yuasa et al.[1] uses connective tissue collected from a posterior

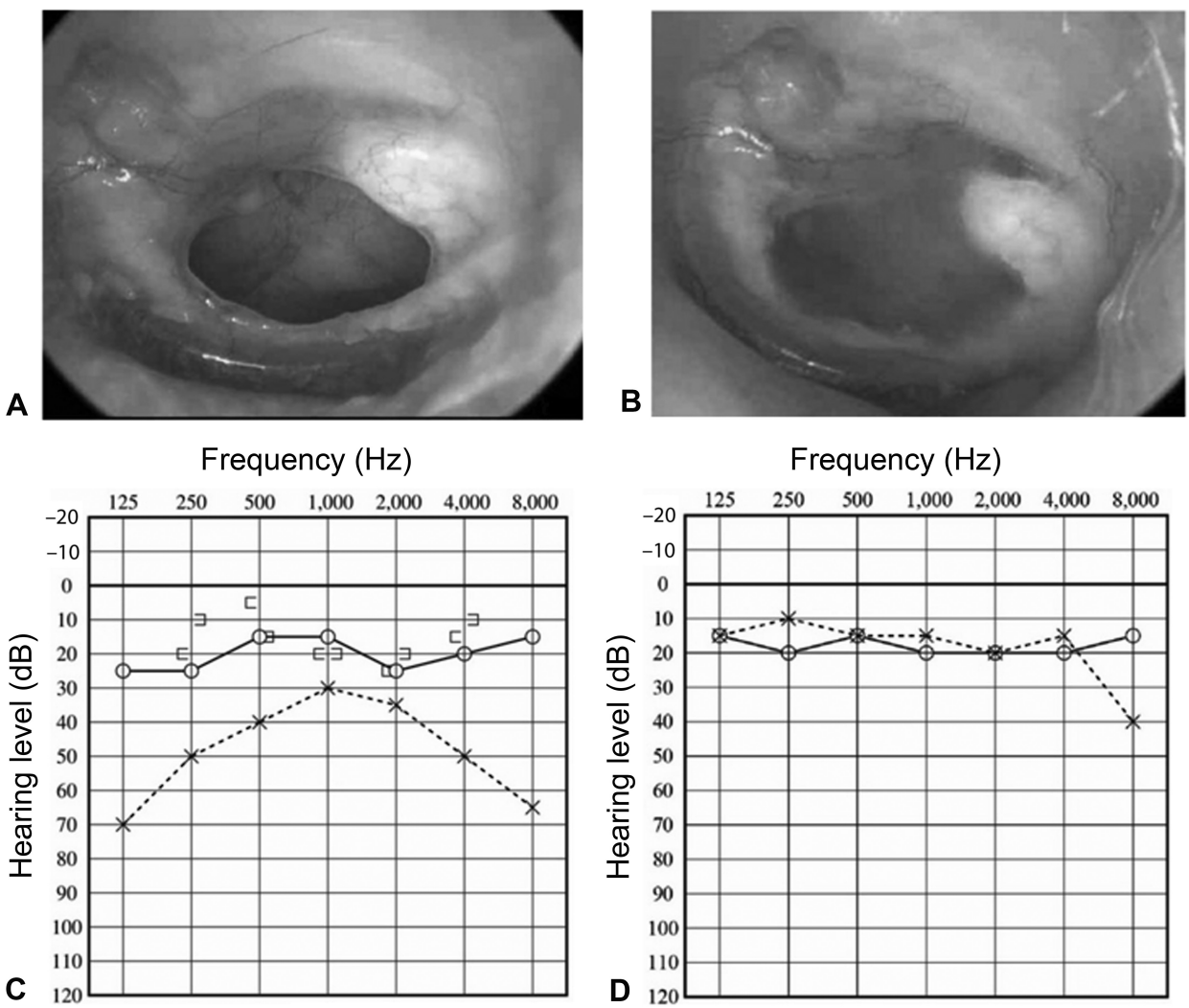


Fig. 5 A case of chronic otitis media of the left ear since childhood (a 58-year-old woman). (**A**) Preoperative left tympanic membrane findings. (**B**) The left tympanic membrane perforation was closed 1 year after surgery. (**C**) Preoperative standard pure tone audiometry findings. (**D**) The mean hearing acuity improved from 33.75 to 16.25 dB 1 year after surgery.

auricular area as the closure material that is fixed to the perforated tympanic membrane using fibrin glue. This procedure is relatively easy, involves minimal patient burden, and has high closure rates; however, this procedure is performed on an inpatient basis at many institutions. Because an incision to a posterior auricular area is required, postoperative wound care is necessary. Moreover, when a blood-derived product, such as fibrin glue, is used, the risk of blood-borne infection cannot be completely eliminated and patients should be informed accordingly.

Nakashima et al.[4] reported a multilayered placement method wherein an oversized autologous tissue is placed on the perforation so that the tissue does not fall into the tympanic membrane perforation. The closure rate of this method was ≤96% (65/68). This surgical procedure is advantageous as fibrin glue is not required; however, general anesthesia is always necessary. Sasaki et al.[2] reported a tympanic membrane perforation–closure technique in which, instead of autologous tissue, a chitin membrane or Teldermis was used in combination with autologous serum ear-drop therapy. The perforation margin was refreshed with 10% silver nitrate, and chitin membrane or Teldermis was used for perforation closure without fibrin glue. Autologous serum-ear drops are prepared from blood collected during surgery and used every 2 weeks after surgery and then instilled into the ear 3–4 times daily. The closure rates with chitin membrane and Teldermis reportedly are 61.8% (34/55) and 72.7% (8/11), respectively. The chitin membrane is an 0.08-mm-thick membrane extracted from red snow crab shells and has been used as a wound-dressing material as it promotes epidermis formation and granulation. Teldermis, which was also used in the current study, is produced from chemical/thermal-treated collagen from young bovine skin. Attachment of Teldermis to mucosal defects in the skin causes the cells to migrate into collagen layers where granulation-like tissue is formed.

In autologous serum ear-drop therapy, a concentrated solution of platelets in the blood is used that contains various cell growth factors. To achieve high wound-healing potential, autologous serum drops are used in various fields, including dentistry, oral surgery, plastic surgery, and ophthalmology. The drops are prepared from a patient's own blood; thus, they are safe and can be easily purified by centrifugation in general clinics.

Teldermis has been used in many other studies.[5–9] Fukami et al.[5] achieved a closure rate of 86% by simply placing Teldermis on perforations refreshed with needles and cotton-swab forceps without using fibrin glue; however, only 27 ears with small perforations (limited to one quadrant) and 3 ears with medium-sized perforations (up to two quadrants) were included; no ears with large perforations were included. Omotehara et al.[6] used Teldermis in combination with a basic fibroblast growth factor preparation (Fiblast spray, Kaken Pharmaceutical Co., Ltd.) and achieved a closure rate of 82.2% (139/169) without using fibrin glue. Shiomi et al.[7] used chitin membrane to fix a bilayer Teldermis to perforations refreshed using OtoLAM or needles in combination with autologous serum and reported a closure rate of 90% (108/118). The method of fixing bilayer Teldermis with a chitin membrane is simple and affordable; thus, we were interested in this method.

Retympa, a kit that includes a basic fibroblast growth factor preparation and gelatin sponge, received insurance coverage in 2019. Kanemaru[10] used Retympa and fibrin glue to achieve a cumulative closure rate of 81% (189/232) after up to four subsequent operations.

Previous reports of tympanic membrane perforation–closure and myringoplasty techniques are summarized in ►**Table 3**, including the methods used to refresh the perforation margin, closure materials, fixation methods, use/nonuse of tissue-regeneration factors, and closure rates.

Our surgical procedure simply uses OtoLAM to refresh the perforation margin and places bilayer Teldermis in the perforation. Among the procedures listed in ►**Table 3**, our method appears to be the simplest one because it does not require autologous tissue collection, fibrin glue, or tissue-regeneration factors. It can be performed as easily as a tympanostomy and a patch test and completed in a short time. The procedure is affordable because neither fibrin glue nor tissue-regeneration factors are used. A major advantage of this method is that fibrin glue is not used, thus eliminating the risk of blood-borne infection and the need to discuss the potential for blood-borne infection with patients. There are fewer obstacles that must be overcome before surgery, and patients do not have strong feelings of resistance toward repeated surgery. Closure rates cannot be compared directly because they are determined using different criteria in different patient populations for successful/failed closure. Nevertheless, sufficient closure rate was achieved with our method despite it being the simplest procedure.

A study by Omotehara et al[6] included 107 patients younger than 70 years and 63 patients ≥71 years and reported that elderly patients accounted for a larger proportion of patients than in any other reports. In our study, 115 patients younger than 70 years and 116 patients ≥71 years were included, and the proportion of elderly patients was significantly higher in our study than in Omotehara et al ($p < 0.05$, chi-squared test). Unless otorrhea or pain occurs repeatedly, unilateral tympanic membrane perforation does not prevent many elderly patients from performing any particular daily activities. Thus, many elderly patients leave unilateral tympanic membrane perforation untreated. We recommend this procedure to such elderly patients without hesitation because it is as simple as tympanostomy, and it may be the reason for many older patients in our study.

Our policy is not to repeat surgery more than three times if the perforation has not shown signs of decrease in size by then; however, surgery is repeated as many times as patients request in some cases because the surgical procedure is simple, the second and subsequent closure attempts are billed to insurers as patch tests (middle-ear function tests: 150 points each), and hearing acuity may improve for a certain period of time even if closure is not achieved. In some cases, closure was achieved after ≥4 operations (6.5%; 15/231) and even after ≥10 operations (2 cases). Patients for whom perforation closure is unsuccessful and who request

Table 3 Summary of previously reported myringoplasty and tympanic membrane perforation closure procedures

Study	Method used for refreshing the perforation margin	Closure material	Method for closure material fixation	Regeneration promotor	Closure rate
Yuasa et al[1]	Perforation margin excision	Autologous tissue	Fibrin glue	None	91.8%
					67/73
Nakashima et al[4]	Perforation margin excision	Autologous tissue	None	None	95.6%
					65/68
Sasaki et al[2]	10% Silver nitrate	Chitin membrane	None	Autologous serum	61.8%
					34/55
	10% Silver nitrate	Terudermis	None	Autologous serum	72.7%
	Perforation margin excision				8/11
Fukami et al[5]	Perforation margin excision	Terudermis	None	None	86.7%
					26/30
Omotehara et al[6]	Perforation margin excision	Terudermis	None	bFGF (Fiblast)	82.2%
					139/169
Shiomi et al[7]	Perforation margin excision	Terudermis	Covered with chitin membrane	Autologous serum	91.5%
	OtoLAM				108/118
Kanemaru[10]	Perforation margin excision	Gelatin sponge	Fibrin glue	bFGF (Retympa)	81.5%
					189/232
This study	OtoLAM	Terudermis	None	None	69.7%
					161/231

surgery on an inpatient basis are referred to nearby institutions with inpatient surgery capabilities.

Conclusion

We described a tympanic membrane perforation–closure procedure using OtoLAM, a carbon dioxide laser tympanostomy device, and Terudermis, a collagen sponge, that can be performed in clinics without inpatient facilities. Although the closure rate after a single operation was not high (33.8%; 78/231), the closure rate increased cumulatively to 69.7% (161/231) by repeating the procedure multiple times. This surgery is advantageous because no time and effort to collect autologous tissue are necessary, the use of OtoLAM simplifies treatment of the perforation margin, and no fibrin glue is required, all of which make the surgery affordable and eliminate the risk of blood-borne infections and the need to inform patients of this possibility.

Funding
None.

Conflict of Interest
None declared.

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