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Concentrated growth factors as a graft material for endoscopic revision tympanoplasty

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This study aims to evaluate the clinical efficacy of concentrated growth factors (CGF) as a graft material in endoscopic revision tympanoplasty for tympanic membrane perforation. A retrospective analysis was conducted on 30 cases of endoscopic revision tympanoplasty performed at the Otolaryngology Department of Shenzhen Nanshan People's Hospital between January 1, 2019, and December 31, 2023. Fifteen patients were assigned to the experimental group, in which CGF was used for perforation repair, while the control group ($n = 15$) received cartilage and perichondrium grafts. Surgical outcomes (intraoperative blood loss, operative time), complications (taste disturbance, ear numbness, postoperative pain, ear fullness, incision infection, etc.), postoperative hearing improvement, and follow-up results (tympanic membrane healing time and healing rate) were statistically analyzed between the two groups. Tympanic membrane perforations in both groups achieved complete healing during follow-up. The experimental group exhibited significantly reduced intraoperative blood loss (15.2 ± 3.8 mL vs. 28.6 ± 5.2 mL; $P = 0.003$), shorter operative time (52.4 ± 10.1 min vs. 78.9 ± 12.6 min, $P = 0.001$), lower postoperative complication rates (0% vs. 26.7%; $P = 0.021$), and accelerated tympanic membrane healing time (14.5 ± 2.3 days vs. 21.8 ± 3.7 days; $P < 0.001$) compared to the control group. However, no significant differences were observed in postoperative hearing outcomes (air-bone gap closure: 12.1 ± 3.5 dB vs. 13.4 ± 4.1 dB; $P = 0.32$) or tympanic membrane healing rates (93.3% vs. 86.7%, $P = 0.48$). Concentrated growth factors are effective and safe as a graft material in endoscopic revision tympanoplasty. CGF is readily available, minimally invasive, and particularly advantageous for use in endoscopic revision tympanoplasty.

Keywords Concentrated growth factors, Graft material, Endoscopic revision tympanoplasty

Abbreviations

ABG	Air-Bone Gap
CGF	Concentrated Growth Factors
ERT	Endoscopic Revision Tympanoplasty
ET	Eustachian Tube
TM	Tympanic Membrane
PTA	Pure-Tone Audiometry
IAIO	International Academy of Implant Osteology
CM	Consensus Meeting
VB	Venous Blood
SVT	Silica-Coated Vacuum Tubes
FG	Fibrin Glue
ETA	Endoscopic Transcanal Approach
TMF	Tympanomeatal flap
P	statistical significance
t-tests	Independent t-tests
χ^2 test	Pearson's chi-square test
FET	Fisher's exact test
IRB	Institutional Review Board
PDGFs	Platelet-Derived Growth Factors

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VEGF	Vascular Endothelial Growth Factor
PRF	Platelet-Rich Fibrin
A-PRF	Advanced Platelet-Rich Fibrin
PPTF	platelet-poor plasma-derived fibrin
AD	alloderm
BCG	Bacterial Cellulose Graft
FEA	Finite Element Analysis
TE	Tissue Engineering
RM	Regenerative Medicine
HA	Hyaluronic Acid
AM	Amniotic Membranes
SA	Synthetic Allografts
IVM	In Vivo Models
PMT	Prospective Multicenter Trials
SCGP	Standardization of CGF Protocols

In recent years, the convergence of heightened emphasis on quality-of-life optimization, escalating demand for minimally invasive surgical interventions, and advancements in precision medicine has propelled endoscopy to the forefront of diagnostic and therapeutic innovations in otology. Endoscopic tympanoplasty, in particular, has emerged as a validated surgical modality, distinguished by its feasibility, safety, and efficacy. This approach offers superior visualization of middle ear anatomy, an expansive operative field, procedural simplicity, and favorable postoperative outcomes, including low complication rates and robust graft survival[1].

Despite these advancements, recurrent tympanic membrane perforations persist in a subset of patients following endoscopic tympanoplasty, attributable to multifactorial etiologies such as systemic comorbidities, technical limitations, and suboptimal postoperative management[2–5]. Such recurrences pose significant clinical challenges, including concerns regarding reoperation success, material availability for repair, surgical morbidity, patient compliance, and cost-effectiveness. Consequently, there is an urgent need for strategies that optimize surgical outcomes while mitigating trauma, reducing healthcare burdens, and preserving auditory function. The selection of graft materials is pivotal in addressing these challenges. Although auricular cartilage remains the conventional choice for primary tympanoplasty[6] its procurement in revision surgeries is often constrained by anatomical limitations and prior tissue utilization. Recent innovations in regenerative medicine have highlighted platelet-derived growth factors(PDGFs) as promising candidates for tissue repair, owing to their angiogenic and proliferative properties[7,8]. Among these, concentrated growth factors (CGF)—a third-generation autologous platelet concentrate—have garnered attention for their fibrin-rich matrix, sustained cytokine release, and demonstrated efficacy in enhancing soft tissue regeneration while minimizing postoperative complications. This unique composition enables CGF to act as a bioactive scaffold, fostering angiogenesis, cellular migration, and tissue regeneration through sustained cytokine release over 7–14 days, closely mimicking the natural healing cascade[9].

This study evaluates a cohort of patients with recurrent tympanic membrane perforations following endoscopic tympanoplasty, rigorously screened through preoperative assessments to include those with mild conductive hearing loss or normal auditory thresholds (Fig. 1). By investigating the clinical efficacy of CGF as a graft material in revision endoscopic tympanoplasty, this work seeks to elucidate its potential in reducing surgical invasiveness, accelerating wound healing, and improving patient-centered outcomes.

Materials and methods

Study design and participants

A retrospective cohort analysis was conducted on 30 patients who underwent endoscopic revision tympanoplasty at the Otolaryngology Department of Shenzhen Nanshan People's Hospital between January 1, 2019, and December 31, 2023. Participants were stratified into two groups: the experimental group ($n = 15$), in which tympanic membrane perforations were repaired using concentrated growth factors (CGF), and the control group ($n = 15$), which received cartilage and perichondrium grafts.

Inclusion Criteria

1. Diagnosis of chronic suppurative otitis media with prior endoscopic tympanoplasty (irrespective of the initial surgical institution).
2. Persistent tympanic membrane perforation (> 3 months postoperatively), confined to ≤ 1 quadrant and sparing the manubrium of the malleus.
3. Normal Eustachian tube function confirmed preoperatively via tubomanometry and the Valsava test. And pure-tone audiometry indicating mild conductive hearing loss (≤ 30 dB) or normal hearing thresholds.
4. Complete clinical records and unilateral pathology.
5. Age ≥ 18 years.

Exclusion Criteria

1. Preoperative temporal bone CT evidence of ossicular chain discontinuity or middle ear soft tissue opacification.
2. Pregnancy, lactation, or comorbidities contraindicating surgery (e.g., coagulopathies, organ dysfunction).
3. Active middle ear malignancy, tuberculous otitis media, or concurrent neurological disorders.

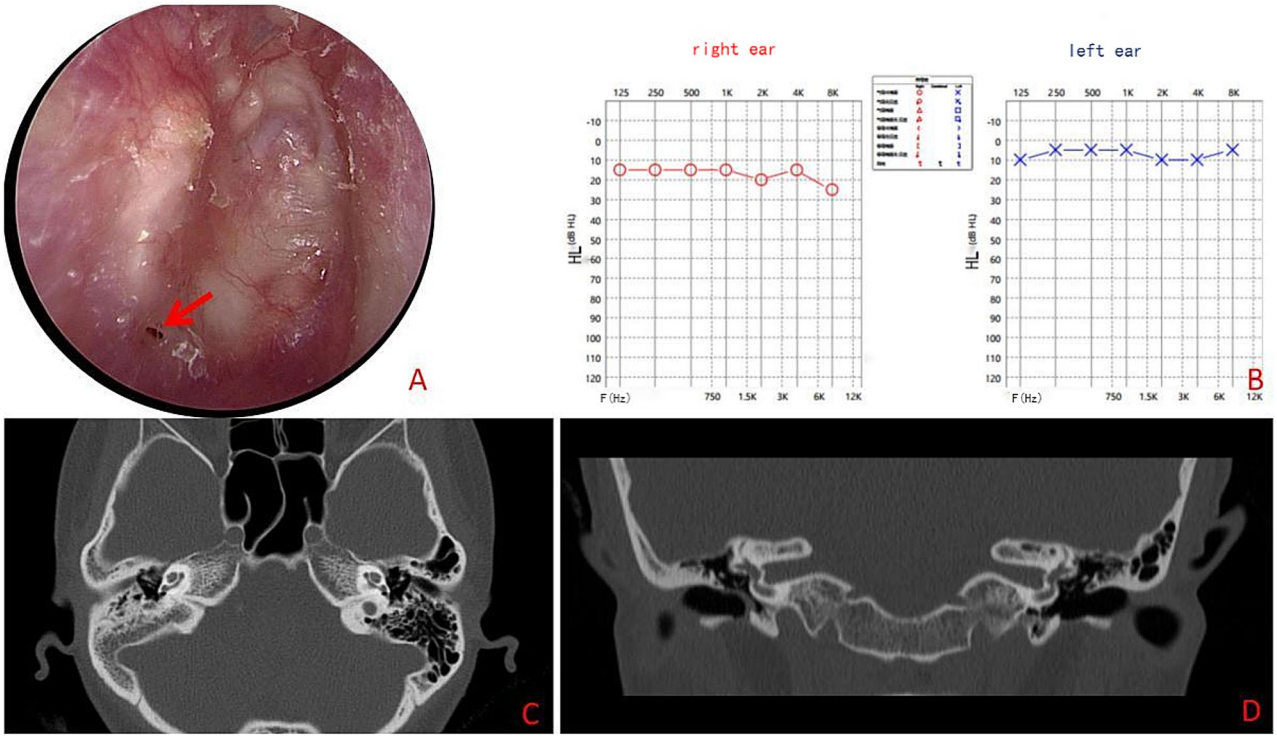

Fig. 1. Preoperative assessment data of typical cases. **(A)** Preoperative endoscope image, with the red arrow indicating the perforated part of the tympanic membrane. **(B)** Preoperative pure tone audiometry suggests normal hearing in the right ear. **(C)** Axial temporal bone CT shows air in the tympanic cavity without any abnormal density shadow. **(D)** Coronal temporal bone CT shows air in the tympanic cavity and an intact ossicular chain.

The patients selected for this study were treated with the proposed protocol in the Department of Otolaryngology, Shenzhen Nanshan People's Hospital. The patients.

were informed about the procedures for the study. Written consent was obtained. The study design and clinical procedures were performed in accordance with the Helsinki Declaration (revised in 2008) and were approved by the The Scientific Research Ethics Committee of Union Shenzhen Hospital, Huazhong University of Science and Technology (Approval No.: KY-2023–081201).

CGF Preparation protocol

The CGF membranes were synthesized following the standardized protocol by Sacco (2006)[10] Venous blood (10 mL) was drawn from the dorsal foot vein using a 21-gauge needle and transferred into sterile silica-coated vacuum tubes (Medifuge®). Tubes were centrifuged at programmed intervals: 30-second acceleration, followed by sequential centrifugation at 2,700 rpm (2 min), 2,400 rpm (4 min), 2,700 rpm (4 min), and 3,000 rpm (3 min), with a 36-second deceleration phase. Post-centrifugation, three distinct layers formed: (1) platelet-poor plasma (discarded), (2) a fibrin-rich CGF intermediate layer containing aggregated platelets and growth factors, and (3) erythrocyte sediment (removed). The CGF layer was promptly harvested under sterile conditions to minimize cytokine degradation. And then we placed the harvested CGF layer on the back of the left hand, and then gently pressed it with the back of the right hand to form a membrane for intraoperative application (Fig. 2).

Surgical procedure

All procedures were performed by a single surgical team under endoscopic guidance.

Control group

Under general anesthesia, the incision of the tragal cartilage was extended to the antitragal notch, and the conchal cartilage and perichondrium were harvested. The graft was thinned and trimmed to size. An endoscopic transcanal approach was employed to prepare the vascular bed at the perforation margin, elevate the tympanomeatal flap, and secure the graft using an underlay technique with fibrin glue.

Experimental group

Two patients underwent surgery under local anesthesia, while 13 received general anesthesia. Concurrent with graft bed preparation via the transcanal approach, venous blood was drawn for CGF membrane synthesis. The vascular bed was meticulously freshened without flap elevation. The CGF membrane was positioned on the inner side of the perforation edge, It adheres to the site relying on the surface tension between the vascular

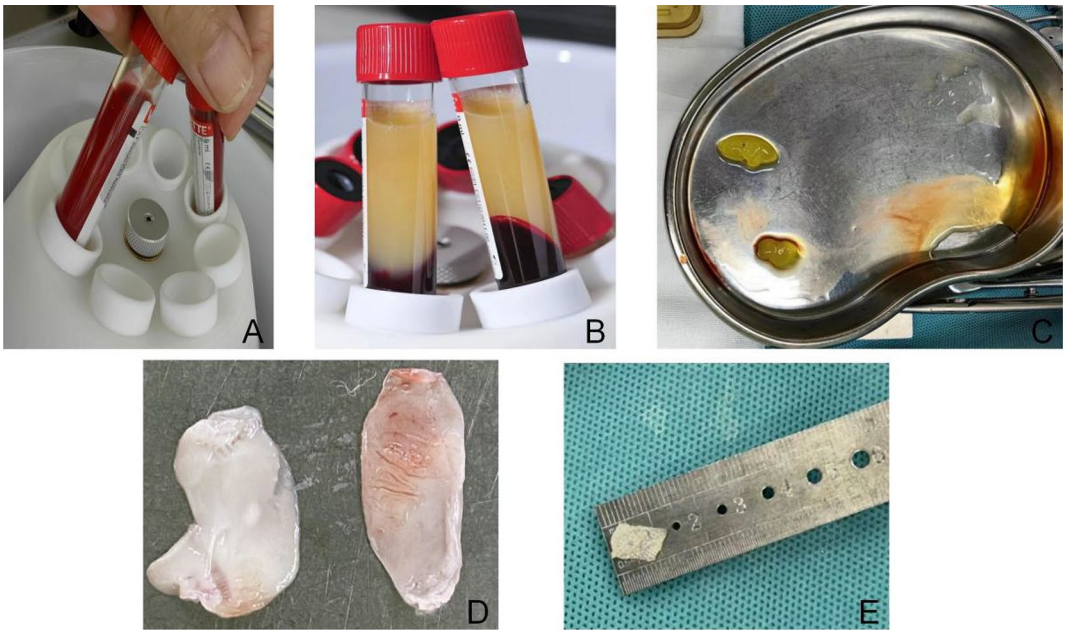

Fig. 2. The Production Process of CGF. **(A)** Venous blood is drawn from the dorsal artery of the patient's foot and placed in a centrifuge. **(B)** The stratified state after centrifugation. **(C)** Retaining the middle CGF layer. **(D)** Compressing the CGF into a membrane. **(E)** The CGF membrane can be trimmed.

bed and the CGF membrane. This fixation method allows the CGF membrane to stably cover the tympanic membrane perforation, facilitating the healing process without the need for additional external fixation means (Fig. 3).

Outcome measures

Primary outcome

The primary outcome was graft success rate, defined as the proportion of patients achieving complete tympanic membrane closure confirmed by endoscopic examination and a type A tympanogram (indicating an intact membrane, aerated middle ear space, and absence of discharge) at the 3-month follow-up.

Secondary outcomes

1. Graft success timing: Time (days) to complete tympanic membrane healing, assessed via endoscopic visualization and absence of air leakage during the Valsalva maneuver.
2. Audiological outcomes: Postoperative improvement in air-bone gap (ABG) at speech frequencies (0.5, 1, 2, and 4 kHz), measured preoperatively and 6 months postoperatively using pure-tone audiometry.
3. Surgical parameters:

   Intraoperative blood loss (mL).
   Total operative time (minutes).

4. Postoperative complications: Incidence of taste disturbance, auricular numbness, pain requiring analgesia, aural fullness, and surgical site infection within 3 months postoperatively.

Statistical analysis

Data were analyzed using SPSS 24.0 (IBM Corp.). Continuous variables (blood loss, operative time, healing time) are expressed as mean ± standard deviation and compared via independent t-tests. Categorical variables (complication rates, success rates) are reported as counts (%) and analyzed using Pearson's chi-square or Fisher's exact test. Statistical significance was defined as $P < 0.05$.

Results

General results

The experimental group comprised 8 males and 7 females, aged 18–42 years, with a mean age of 29.60 ± 7.50 years. The control group included 7 males and 8 females, aged 19–45 years, with a mean age of 30.33 ± 7.21 years. No statistically significant differences in baseline characteristics were observed between the two groups ($P > 0.05$), indicating comparability.

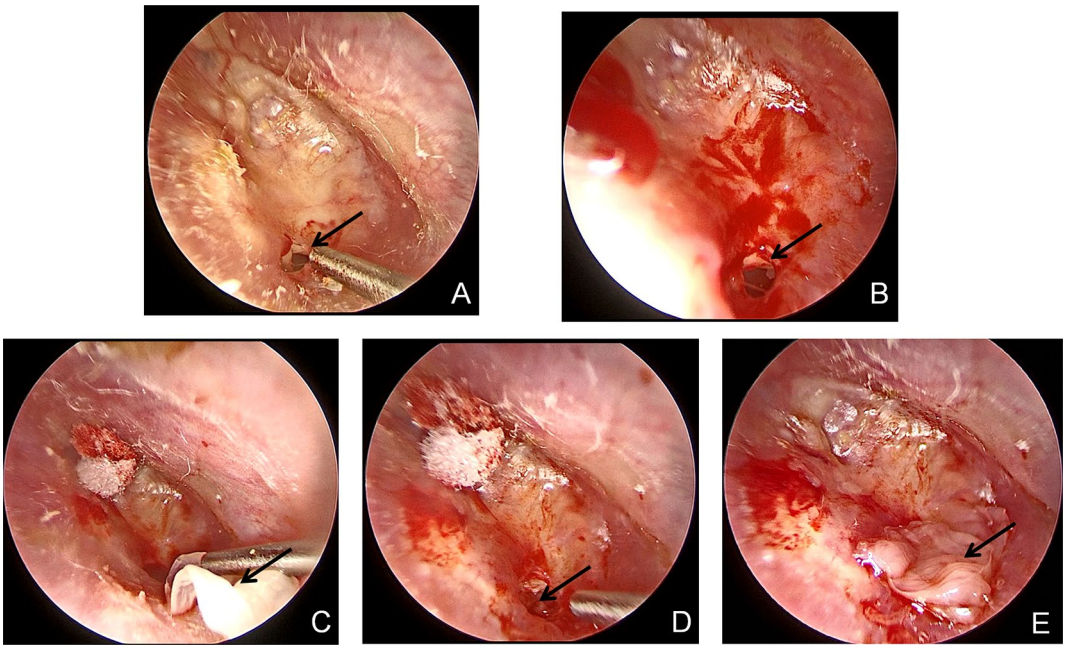

Fig. 3. Surgical Procedure of the Experimental Group. **(A)** Remove the scab on the surface of the perforation. The black arrow indicates the perforation. **(B)** Prepare the vascular bed. **(C)** Place the CGF membrane (indicated by the black arrow) in the inner side of the perforation. **(D)** The state at the end of the operation. The black arrow indicates the CGF membrane located in the inner side of the perforation. **(E)** A CGF membrane (indicated by the black arrow) was placed on the epithelial layer of the tympanic membrane perforation to reduce bleeding. It can be removed on the first day after the operation to observe the recovery of the perforation.

Group	Healing Time (days)	Healing Rate (*n*/%)
Experimental ($n = 15$)	8.20 ± 0.225	15(100%)
Control ($n = 15$)	13.58 ± 0.826	15(100%)
χ^2	0.366	0
P-value	$p<0.05$	$p>0.05$

Table 1. Comparison of postoperative tympanic membrane healing time and healing rate.

Primary outcome: graft success rate

Complete tympanic membrane closure, confirmed by endoscopic examination and type A tympanogram (indicating an intact membrane, aerated middle ear, and absence of discharge), was achieved in 93.3% (14/15) of the experimental group (CGF) and 86.7% (13/15) of the control group at the 3-month follow-up. No statistically significant difference in graft success rate was observed between the two cohorts ($P = 0.48$, Fisher's exact test) (Table 1).

Secondary outcomes

Graft success timing

The experimental group demonstrated a significantly shorter time to complete tympanic membrane healing compared to the control group. Full closure, defined as the absence of air leakage during the Valsalva maneuver, was achieved at 14.5 ± 2.3 days in the CGF group versus 21.8 ± 3.7 days in the temporalis fascia group ($P < 0.001$, independent t-test) (Table 1).

Audiological outcomes

Postoperative air-bone gap (ABG) closure at speech frequencies (0.5–4 kHz) improved comparably in both groups. The mean ABG reduction was 12.1 ± 3.5 dB in the experimental group and 13.4 ± 4.1 dB in the control group, with no statistically significant intergroup difference ($P = 0.32$, independent t-test). However, there was a significant statistical difference in hearing improvement at the low-frequency of 0.5 kHz between the two groups, with the experimental group demonstrating a markedly superior improvement in air-bone gap (ABG) at 0.5 kHz compared to the control group. (Table 2)

Group	Preoperative ABG (dB HL)					Postoperative ABG (dB HL)				
	0.5 K	1 K	2 K	4 K	AVER	0.5 K	1 K	2 K	4 K	AVER
Experimental (n = 15)	4.79 ± 0.56	12.52 ± 0.77	12.61 ± 0.89	12.68 ± 1.01	12.60 ± 0.98	1.81 ± 0.44	3.09 ± 0.55	3.12 ± 0.64	3.14 ± 0.75	3.13 ± 0.63
Control (n = 15)	5.23 ± 0.67	12.63 ± 1.02	12.72 ± 0.91	12.81 ± 1.12	12.53 ± 14.76	2.22 ± 0.56	3.42 ± 0.67	3.51 ± 0.78	3.59 ± 0.89	3.53 ± 0.98
P-value	p<0.05	p>0.05	p>0.05	p>0.05	p<0.05	p<0.05	p>0.05	p>0.05	p>0.05	p<0.05

Table 2. Comparison of postoperative hearing effects between the two groups.

Group	Intraoperative Blood Loss (ml)	Operation Time (min)
Experimental (n = 15)	2.00 ± 0.93	45.05 ± 12.94
Control (n = 15)	0.20 ± 0.88	19.98 ± 12.16
χ^2	1.472	9.6
P-value	p<0.05	p<0.05

Table 3. Comparison of surgical indicators between the two groups.

Group	Taste Changes	Ear Numbness	Postoperative Pain	Ear Fullness	Incision Infection	Total Complications
Experimental (n = 15)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Control (n = 15)	1(6.7%)	3(20%)	2(13.3%)	3(20%)	0(0%)	9(60%)
χ^2						12.858
P-value						p<0.05

Table 4. Comparison of complication incidence during treatment between the two Groups(n/%).

Surgical parameters

Intraoperative blood loss was markedly reduced in the experimental group (15.2 ± 3.8 mL) relative to the control group (28.6 ± 5.2 mL, P = 0.003).Operative time was significantly shorter in the CGF cohort (52.4 ± 10.1 min) compared to the temporalis fascia group (78.9 ± 12.6 min) (Table 3).

Postoperative complications

No complications—including taste disturbance, auricular numbness, pain requiring analgesia, aural fullness, or surgical site infection—were reported in the experimental group. In contrast, the control group exhibited a 26.7% (4/15) complication rate (P = 0.021, Fisher's exact test), comprising transient taste changes (1 case), auricular numbness (3 cases), mild pain (2 cases), and aural fullness (3 cases). All adverse events resolved spontaneously or with conservative management within 4 months (Table 4).

Discussion

Advantages of CGF in revision endoscopic tympanoplasty

The present study demonstrates that concentrated growth factors (CGF) offer distinct advantages in revision endoscopic tympanoplasty, particularly in reducing surgical invasiveness and accelerating tympanic membrane healing. The experimental group exhibited significantly shorter operative time (52.4 vs. 78.9 min, P = 0.001) and reduced intraoperative blood loss (15.2 vs. 28.6 mL, P = 0.003) compared to cartilage and perichondrium grafts. These findings align with the inherent properties of CGF, which eliminates the need for donor site harvesting, thereby minimizing tissue trauma and procedural complexity[11].Furthermore, the absence of postoperative complications in the CGF group-such as taste disturbance, auricular numbness, or surgical site infection—contrasts sharply with the 26.7% complication rate observed in the control group (P = 0.021). This aligns with prior studies highlighting CGF's biocompatibility and anti-inflammatory properties, which mitigate adverse events associated with traditional grafts[8,12].Notably, CGF's fibrin-rich matrix facilitates sustained cytokine release (e.g., vascular endothelial growth factor(VEGF), platelet-derived growth factor (PDGF)) over 7–14 days, mimicking the natural healing cascade[9,13].This bioactive scaffold promotes angiogenesis and epithelial migration, explaining the accelerated healing time observed in the experimental group (14.5 vs. 21.8 days, P < 0.001). Such outcomes are comparable to platelet-rich fibrin (PRF), another autologous concentrate, though CGF's denser fibrin network may confer superior mechanical stability, as suggested by in vitro studies[14].

Comparative efficacy against alternative graft materials

Although autologous tissues such as cartilage remain the gold standard for tympanic membrane repair[15–17], their limitations in revision surgeries (e.g., donor site scarcity, anatomical constraints, and procedural morbidity) necessitate exploration of alternative materials[11]. The repair materials for the tympanic membrane have always been a hot topic in various research fields[18–27]. Recent advancements in regenerative medicine have introduced options like hyaluronic acid (HA) patches, amniotic membranes, and synthetic allografts[21–23].However, these

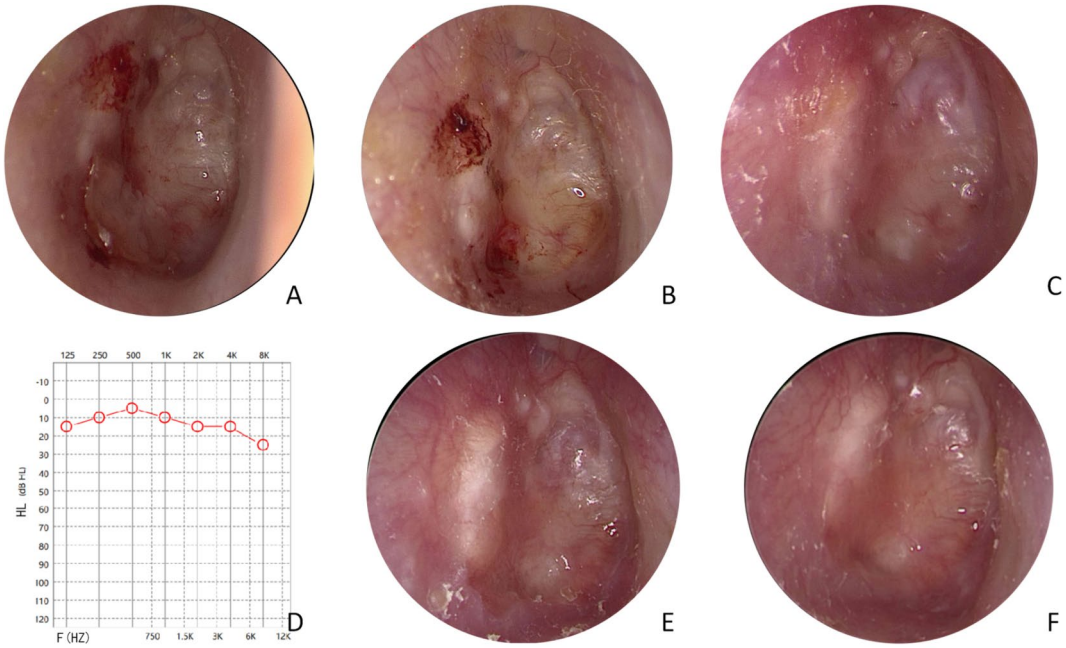

Fig. 4. Postoperative Follow-up Information of a Typical Case. **(A)** On the first day after the operation, the endoscopic image showed that the surface of the tympanic membrane perforation was covered by a CGF membrane, and the CGF membrane was removed then. **(B)** On the 3rd day after the operation, a blood scab was observed covering the surface of the perforation. **(C)** On the 7 th day after the operation, the tympanic membrane was found to be healed and epithelialized. **(D)** The hearing was normal during the reexamination one month after the operation. **(E)** The endoscopic image at the 3rd month after the operation showed that the right tympanic membrane was intact. **(F)** The endoscopic image at the 6 th month after the operation revealed that the right tympanic membrane remained intact.

alternatives present distinct trade-offs in clinical applicability. Hyaluronic acid-based scaffolds, for instance, exhibit excellent biocompatibility and promote epithelial migration but lack mechanical resilience, often requiring reinforcement with other materials to prevent graft displacement[24].Similarly, amniotic membranes, though rich in growth factors and anti-inflammatory properties, face ethical concerns, limited availability, and potential immunogenicity despite decellularization protocols[25,26].Synthetic allografts (e.g., silicone, polyurethane) provide structural support but fail to integrate bioactive components critical for natural healing, increasing risks of infection or extrusion[27].In contrast, CGF combines autologous origin (eliminating immunogenicity) with a biodegradable fibrin matrix that sustains growth factor delivery[9,13].This contrasts sharply with HA patches or synthetic materials, which lack sustained growth factor delivery[28].Furthermore, CGF eliminates donor site morbidity, a significant drawback of autologous fascia or cartilage harvesting[11].Notably, CGF's efficacy in reducing operative time and complications aligns with outcomes reported for platelet-rich fibrin (PRF), another autologous concentrate[8].This dual mechanism not only accelerates healing but also reduces reliance on external biocompatible materials. Compared to PRF, CGF's slower degradation rate may enhance its utility in revision surgeries requiring prolonged mechanical support[14].These properties position CGF as a superior choice in revision surgeries where minimal invasiveness and rapid healing are prioritized, particularly when autologous tissues are unavailable or contraindicated. Follow-up for at least one year revealed no cases of rejection or re-perforation (Fig. 4).

Limitations and future directions

Despite its promise, this study has limitations. First, the retrospective design and small sample size ($n = 30$) limit generalizability, though post-hoc power analysis confirmed adequacy for primary endpoints. Second, CGF's long-term mechanical stability remains unverified, as current degradation studies rely on simulated physiological fluids rather than in vivo models[29]. Third, while two cases in the experimental group utilized local anesthesia, the majority (13/15) required general anesthesia. This precludes definitive conclusions about CGF's compatibility with localized protocols, necessitating prospective trials to evaluate patient tolerance and cost-effectiveness.

Conclusions

This study demonstrates that CGF are a safe and effective graft material for endoscopic revision tympanoplasty. Compared to cartilage and perichondrium, CGF significantly reduces intraoperative blood loss, shortens operative time, and eliminates postoperative complications. The accelerated healing time reflects CGF's regenerative potential through sustained cytokine release and fibrin-rich scaffolding. While long-term hearing

outcomes and final healing rates were comparable, CGF's procedural efficiency and reduced morbidity make it ideal for revision cases, particularly when donor site limitations exist.

Future research should prioritize prospective multicenter trials to validate long-term graft stability and cost-effectiveness. Standardization of CGF protocols may further advance minimally invasive, patient-centered approaches in tympanoplasty.

Data availability

The datasets used and analysed during the current study available from the corresponding author on reasonable request.

Received: 23 February 2025; Accepted: 15 May 2025
Published online: 19 May 2025

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Acknowledgements

Thank you for all authors and grants from the Nanshan District Medical Key Discipline Construction Financial Support Project, Shenzhen Municipal Science and Technology Innovation Committee under Grant JCYJ20230807093701003; and Guangdong High-level Hospital Construction.

Author contributions

Nan Zeng was responsible for designing the theme. Nan Zeng, Lue Zhang and Qiong Yang were responsible for data collection and surgical procedures. Jing Hu, Yubo Jin, and Shuyi Hong prepared figures and tbales. Because this research is designed and carried out under the guidance of Shang Yan, he is the correspondence author. All authors reviewed the manuscript.

Funding

This study was supported by grants from the Nanshan District Medical Key Discipline Construction Financial Support Project, Shenzhen Municipal Science and Technology Innovation Committee under Grant JCYJ20230807093701003; and Guangdong High-level Hospital Construction.

Declarations

Consent for publication

Written informed consent for publication of their clinical details and clinical images was obtained from the patient.

Competing interests

The authors declare no competing interests.

Additional information

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