HEAD AND NECK SURGERY AND ONCOLOGY
ORIGINAL ARTICLE
DOI: 10.5152/B-ENT.2026.262056

Comparative Effects of Platelet-Rich Plasma, Prostaglandin E1, and Dexpanthenol on Wound Healing in an Experimental Pharyngocutaneous Fistula Model

Ali Adnan Özdemir[1], Tuncay Tunçcan[2], Caner Kılıç[2], Felat Toprak[2], Bayram Barış Büyük[2], Gülay Bilir Dilek[2]

[1]Ordu Training and Research Hospital, Department of Otolaryngology, Ordu, Türkiye
[2]University of Health Sciences, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Department of Otolaryngology, Ankara, Türkiye

Cite this article as: Özdemir AA, Tunçcan T, Kılıç C, Toprak F, Büyük BB, Dilek GB. Comparative effects of PRP, PGE1, and dexpanthenol on wound healing in an experimental pharyngocutaneous fistula model. B-ENT. 2026, 22, 2056, doi:10.5152/B-ENT.2026.262056.

ABSTRACT

Objective: Pharyngocutaneous fistula (PCF) remains a major complication after laryngopharyngeal surgery. Experimental data investigating potential therapeutic agents for improving PCF healing are limited. This study aimed to establish a reproducible rat model of PCF and to evaluate the effects of platelet-rich plasma (PRP), prostaglandin E1 (PGE1), and dexpanthenol on wound healing using macroscopic and histopathological parameters.

Methods: Twenty-eight female Sprague–Dawley rats were randomly assigned to 4 groups, each containing 7 rats. A standardized pharyngeal perforation was created for PCF and left to heal. The first group was the control group. Groups 2, 3, and 4 received PRP, PGE1, and dexpanthenol, respectively, by local application to the fistula wound bed during surgery, followed by once-daily local wound-bed application for 6 consecutive days. All rats corresponding to all groups were sacrificed on the seventh day. They were evaluated macroscopically and histopathologically.

Results: Macroscopic evaluation showed that fistula opening was less frequent in the PRP group than in the control group. Histopathological evaluation demonstrated more favorable wound-healing parameters, particularly increased collagen deposition and altered inflammatory cell density, mainly in the PRP and dexpanthenol groups.

Conclusion: Platelet-rich plasma greatly improved the healing parameters in the experimental PCF model. Prostaglandin E1 and dexpanthenol also showed positive effects. These findings indicate possible therapeutic roles; however, clinical studies are necessary to validate their applicability.

Keywords: Dexpanthenol, pharyngeal fistula, platelet-rich plasma, prostaglandins E, rats, wound healing

Introduction

A pharyngocutaneous fistula (PCF) is a complication that occurs more frequently following a total laryngectomy; furthermore, it is a complication that can occur following pharyngeal and hypopharyngeal tumour surgery.[1] Pharyngocutaneous fistula occurs when there is leakage of saliva from the closed areas of the pharynx, resulting in fluid accumulation between the pharynx and the skin. In a study by Busoni et al,[2] 62.8% of patients who developed PCF were managed conservatively, whereas 37.2% required advanced surgical intervention.

Several risk factors have been associated with postoperative PCF formation, including previous radiotherapy or chemotherapy, blood transfusion, subglottic laryngeal cancer, T-shaped pharyngeal closure, chronic obstructive pulmonary disease, smoking, anemia, and malnutrition.[3]

Platelet-rich plasma (PRP) is an autologous blood-derived product containing a high concentration of platelets, growth factors, and bioactive proteins that contribute to tissue repair and regeneration. It facilitates the migration, proliferation, and differentiation of cells implicated in tissue regeneration.[4] In vitro studies have shown that applying PRP leads to more

Corresponding author: Ali Adnan Özdemir, e-mail: dr.aliadnanozdemir@gmail.com
Received: May 23, 2026 **Revision Requested:** June 10, 2026 **Last Revision Received:** June 24, 2026 **Accepted:** July 23, 2026 **Publication Date:** August 17, 2026
Available online at www.b-ent.be

CC BY 4.0: Copyright@Author(s), "Content of this journal is licensed under a Creative Commons Attribution 4.0 International License."

mesenchymal stem cells, more fibroblast growth, and more collagen production, which speeds up the healing of wounds.[5] Prostaglandin E1 safeguards against ischemia-reperfusion injury by regulating the release of pro-inflammatory and anti-inflammatory cytokines. It enhances oxygenation and glucose delivery to tissues and modulates their absorption in ischemic tissues, potentially expediting the healing process.[6] Dexpanthenol, a precursor of pantothenic acid (vitamin B5), promotes epithelial formation and regeneration.[7] Experimental studies demonstrate enhanced fibroblast proliferation, collagen synthesis, cell migration, and adhesion in cultures supplemented with pantothenic acid derivatives.[8]

Although clinically significant, experimental investigations on PCF are scarce and primarily concentrate on risk factors. In addition to their experimental relevance, these agents are already used in various clinical settings, suggesting potential applicability in head and neck surgery for improving postoperative wound healing and reducing fistula-related morbidity. The current study sought to develop an experimental PCF model in rats and to assess the impacts of PRP, PGE1, and dexpanthenol on healing through macroscopic and microscopic parameters.

Methods

Study Design and Animals

This experimental study was approved by the institutional animal ethics committee and conducted at the XXX Experimental Animal Research Center. Thirty-one female Sprague–Dawley rats were used in the study. Of these, 28 rats were allocated to the experimental groups, and 3 additional rats were used as blood donors for PRP preparation. During the postoperative follow-up period, 1 rat in the control group and 1 rat in the dexpanthenol group died and were excluded from the final analysis. Therefore, the final analysis included 26 rats: 6 in the control group, 7 in the PRP group, 7 in the PGE1 group, and 6 in the dexpanthenol group. Sprague–Dawley rats (3-6 months old, weighing 300-400 g) were individually housed under controlled environmental conditions (21-24°C, 50% humidity, and a 12-hour light/dark cycle) with unrestricted access to food and water.

Anesthesia and Surgical Procedure

General anesthesia was induced by intraperitoneal administration of ketamine (40-90 mg/kg) and xylazine (5-10 mg/kg). A preliminary study was conducted prior to the main experiment, in which, a pilot procedure was performed in 3 rats to optimize the PCF creation technique. In the pilot model, a transoral pediatric nasogastric tube was used to identify the incision site. However, this approach resulted in respiratory compromise and severe postoperative local complications, including cervical edema, purulent discharge, tissue necrosis, and feeding difficulty. Therefore, this technique was not used in the main experiment, and a controlled perforation using a 2.10-mm intravenous catheter was preferred.

Main Points

- A standardized and reproducible experimental rat model of pharyngocutaneous fistula (PCF) was successfully established.
- Platelet-rich plasma (PRP) significantly reduced fistula formation and improved both macroscopic and histopathological healing parameters.
- Prostaglandin E1 and dexpanthenol also enhanced wound healing, particularly by increasing collagen deposition and neoangiogenesis.
- Among the tested agents, PRP showed the most consistent and pronounced therapeutic effect.
- These findings suggest that PRP may have potential clinical value as an adjunctive treatment to improve wound healing and reduce PCF risk.

After shaving and sterile preparation, the rats were placed in the supine position with neck extension. A 2-cm midline cervical incision was made. The submandibular glands and sternothyroid muscles were retracted to expose the hypopharynx and cervical esophagus. A perforation between these structures was created using a 2.10-mm intravenous catheter to establish the PCF model (Figure 1). Bleeding was controlled, and the skin incision was closed with 4-0 silk sutures. Pilot experiments confirmed that this perforation reliably produced the PCF model.

Randomization

The animals were randomly assigned to 4 experimental groups. Randomization was performed using a simple random allocation method by an investigator who was not involved in the outcome assessment. The standard PCF model was established in all rats by a single researcher, and the animals were monitored for 7 days.

Sample Size

Sample size was calculated using G*Power version 3.1 (effect size = 0.70, $\alpha = 0.05$, power = 80%), which indicated that a minimum of 28 animals was required.

Experimental Groups

Group 1 (control group, n = 7): The control group consisted of the standard PCF model. No treatment was administered, and only observation was performed during the study period.

Group 2 (PRP group, n = 7 + 3 donor rats): Platelet-rich plasma was prepared from 3 donor rats under general anesthesia. Whole blood (10 mL per rat) was obtained by intracardiac puncture using a 21-G syringe and transferred into PRP tubes. Samples were centrifuged at 1500 rcf for 7 minutes at 22°C, resulting in 3 layers: erythrocytes, buffy coat, and plasma. The plasma and buffy coat were collected and centrifuged again at 1500 rcf for 9 minutes under the same conditions. Approximately 2 mL of PRP was obtained from 10 mL of whole blood. Platelet counts were not measured; however, the standardized preparation protocol was consistent with previously described experimental PRP methods. Previous experimental studies have demonstrated that similar double-centrifugation protocols yield platelet concentrations sufficient to exert biological activity, supporting the validity of the PRP preparation used in this study.[9] Platelet-rich plasma was kept at room temperature (20-25°C) until use. The PCF model was established in all rats. During surgery, 0.1 mL PRP was applied to the fistula wound bed. The same dose was then applied locally to the fistula wound bed once daily for 6 consecutive postoperative days.

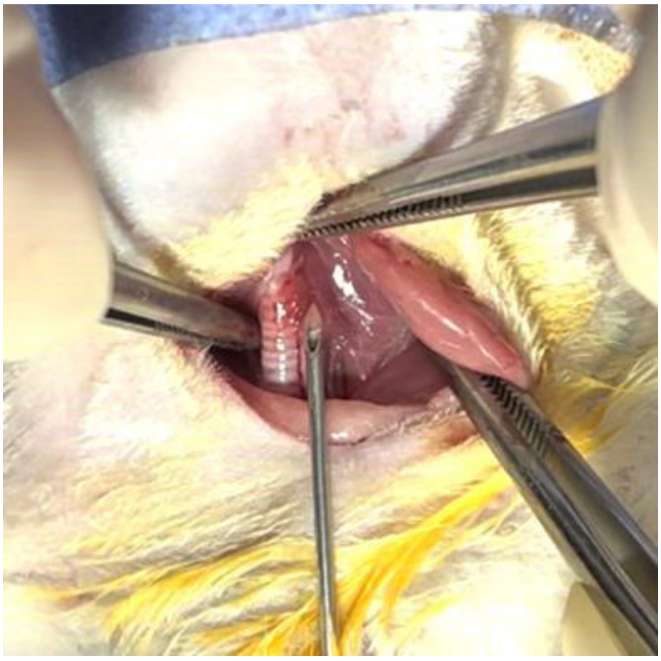

Figure 1. Perforation made with an intravenous catheter between the hypopharynx and the cervical oesophagus.

Group 3 (PGE1 group, n = 7): Anesthesia was induced intraperitoneally. The PCF model was created in all rats as in the control group. Intraoperatively, PGE1 (Jectera 20 mcg/mL ampoule—Vem İlaç San. ve Tic. A.Ş.) at a dose of 2 micrograms (0.1 mL) was administered to the fistula wound bed. The same dose was then applied locally to the fistula wound bed once daily for 6 consecutive postoperative days.

Group 4 (Dexpanthenol group, n = 7): Anesthesia was induced intraperitoneally. The PCF model was established in all rats as in the control group. During surgery, 2.5 mg (0.1 mL) of dexpanthenol (Bepanthen 500 mg/2 mL ampoule—Bayer Türk Kimya San. Ltd. Şti.) was administered to the fistula wound bed. The same dose was then applied locally to the fistula wound bed once daily for 6 consecutive postoperative days.

Euthanasia

All rats were euthanized 7 days after surgery using a high-dose anesthetic.

Macroscopic Evaluation

Fistula was considered absent when the pharyngoesophageal perforation site was completely closed and mucosal continuity was restored. Fistula was considered present when the perforation site remained open and was accompanied by visible leakage and/or food residue in the wound area. The cervical region was examined for the presence of a fistula opening, saliva leakage, abscess formation, and ulceration..

Histopathological Evaluation

Following euthanasia, an en bloc tissue sample was obtained from the surgical site in each animal. The harvested specimens included the skin, subcutaneous tissue, pharyngeal wall, fistula tract, and adjacent wound bed. All samples were fixed in 10% formaldehyde for 24 hours before tissue processing. Representative sections containing the fistula tract and surrounding tissues were then prepared for histopathological evaluation. The specimens were embedded in paraffin blocks, sectioned at a thickness of 4 mm, and stained with hematoxylin–eosin and Giemsa. The procedure involved a microscopic analysis by a pathologist. The pathologist was blinded to group allocation. The assessment of angiogenesis, the presence of granulation tissue, collagen formation, fibroblast quantity, and inflammation severity was conducted microscopically using the Ehrlich Hunt scale.[10] The presence of epithelial regeneration was also examined.

Inflammatory cells, fibroblasts, and granulocytes were evaluated at high magnification. Inflammation was graded as minimal (<10%), mild (11%-25%), moderate (26%-50%), or severe (>50%). Collagen deposition was classified as absent, minimal, moderate, or extensive. Angiogenesis was assessed by counting capillaries in a high-power field and graded as absent, mild (<5 vessels), moderate (5-10 vessels), or intense (>10 vessels). Epithelial regeneration was recorded as absent or present (partial or complete).

Ethical Approval

The study was approved by the Gülhane Animal Experiments Ethics Committee on October 31, 2023 with approval number ETLIK-2023/23 and was conducted in accordance with institutional animal research guidelines.

Statistical Analysis

Categorical variables were expressed as number and percentage. Normality was assessed using the Shapiro–Wilk test. As group sizes were <30, non-parametric tests were applied. Continuous and ordinal variables were presented as median (min–max). Comparisons between 2 groups were performed using the Mann–Whitney *U*-test, and comparisons among more than 2 groups using the Kruskal–Wallis test. Statistical analyses were conducted with IBM SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA). A P value < .05 was considered statistically significant.

Results

During the postoperative follow-up period, 1 rat in the control group and 1 rat in the dexpanthenol group died and were excluded from the final analysis. Therefore, 26 rats were included in the final analysis. The exact cause of death could not be determined.

Macroscopic findings are summarized in Table 1. Abscess formation was observed in 66.7% of the control group, 42.9% of the PRP group, 28.6% of the PGE1 group, and 33.3% of the dexpanthenol group. Ulceration was less frequent in the PRP group than in the control group. Similarly, fistula opening was observed less frequently in the PRP and dexpanthenol groups compared with the control group. Overall, fistula opening differed among the groups, with the lowest frequencies observed in the PRP and dexpanthenol groups.

Histopathological findings are summarized in Table 2. Compared with the control group, collagen deposition was higher in the PRP, PGE1, and dexpanthenol groups ($P = .01$, $P = .001$, and $P = .002$, respectively). Among the treatment groups, collagen deposition was higher in the PGE1 and dexpanthenol groups than in the PRP group ($P = .03$ and $P = .01$, respectively).

Table 1. Macroscopic Findings and Intergroup Comparisons Among Experimental Groups

Macroscopic Finding	Group 1 Control n/N (%)	Group 2 PRP n/N (%)	Group 3 PGE1 n/N (%)	Group 4 Dexpanthenol n/N (%)	Overall *P**	Pairwise Comparisons*
Abscess formation	4/6 (66.7)	3/7 (42.9)	2/7 (28.6)	2/6 (33.3)	.64	G1 vs. G2: 0.59 G1 vs. G3: 0.28 G1 vs. G4: 0.56 G2 vs. G3: 1.00 G2 vs. G4: 1.00 G3 vs. G4: 1.00
Ulceration	5/6 (83.3)	1/7 (14.3)	4/7 (57.1)	3/6 (50.0)	.10	G1 vs. G2: **0.02** G1 vs. G3: 0.55 G1 vs. G4: 0.54 G2 vs. G3: 0.26 G2 vs. G4: 0.26 G3 vs. G4: 1.00
Fistula opening	5/6 (83.3)	1/7 (14.3)	3/7 (42.9)	1/6 (16.7)	**.05**	G1 vs. G2: **0.02** G1 vs. G3: 0.26 G1 vs. G4: 0.80 G2 vs. G3: 0.55 G2 vs. G4: 1.00 G3 vs. G4: 0.55

*Fisher's exact test was used for overall and pairwise comparisons.
G1, control group; G2, PRP group; G3, PGE1 group; G4, dexpanthenol group; PGE1, prostaglandin E1; PRP, platelet-rich plasma.
Bold values indicate statistically significant results.

Fibroblast density was higher in the PRP and PGE1 groups than in the control group ($P = .04$ and $P = .05$, respectively). Neoangiogenesis was more prominent in the PGE1 and dexpanthenol groups compared with the control group ($P = .02$ and $P = .03$, respectively). Mononuclear cell density was higher in the PRP group than in the control and PGE1 groups ($P = .02$ and $P = .01$, respectively). Mononuclear cell density was also higher in the dexpanthenol group than in the PGE1 group ($P = .03$). Granulocyte density was higher in the PRP and dexpanthenol groups than in the control group ($P = .01$ and $P = .007$, respectively). In the overall comparison, collagen deposition, mononuclear cell density, and granulocyte density differed among the groups ($P < .001$, $P = .01$, and $P = .02$, respectively).

Representative histopathological findings of epithelialization, collagen deposition, fibroblast proliferation, inflammatory cell infiltration, and neoangiogenesis are presented in Figure 2 (A-F).

Discussion

Conservative management of PCF aims to promote fistula closure by enhancing local perfusion and granulation tissue formation. Platelet-rich plasma, PGE1, and dexpanthenol—3 agents with distinct biological mechanisms affecting tissue repair—were therefore assessed in this work. With a reported prevalence of 28.9%, PCF is still a serious complication following salvage laryngectomy, leading to prolonged hospitalization and increased costs.[11,12]

Although experimental PCF models are uncommon, Weiss et al[13] provided an early framework for modelling fistula formation in animals by excising part of the thyrohyoid

Table 2. Histopathological Comparison Between Groups

Comparison	Epithelialization (*P*)	Collagen Deposition (*P*)	Fibroblast Density (*P*)	Mononuclear Cell Density (*P*)	Granulation Tissue (*P*)	Neoangiogenesis (*P*)
G1 vs. G2	.59	**.01**	**.04**	**.02**	**.01**	.24
G1 vs. G3	.26	**.001**	.05	.80	.18	**.02**
G1 vs. G4	.54	**.002**	.26	.05	**.007**	**.03**
G2 vs. G3	1.00	**.03**	.65	**.01**	.36	.47
G2 vs. G4	1.00	**.01**	.18	.17	.21	.42
G3 vs. G4	1.00	.40	.29	**.03**	.11	.85
All groups	.56	**<.001**	.09	**.01**	**.02**	.10

Values are presented as *P* values. Bold values indicate statistically significant results.
P values for epithelialization were calculated using Fisher's exact test. *P* values for collagen deposition, fibroblast density, mononuclear cell density, granulation tissue, and neoangiogenesis were calculated using the Mann–Whitney *U*-test for pairwise comparisons and the Kruskal–Wallis test for overall comparisons.
G1, control group; G2, PRP group; G3, PGE1 group; G4, dexpanthenol group; PGE1, prostaglandin E1; PRP, platelet-rich plasma.

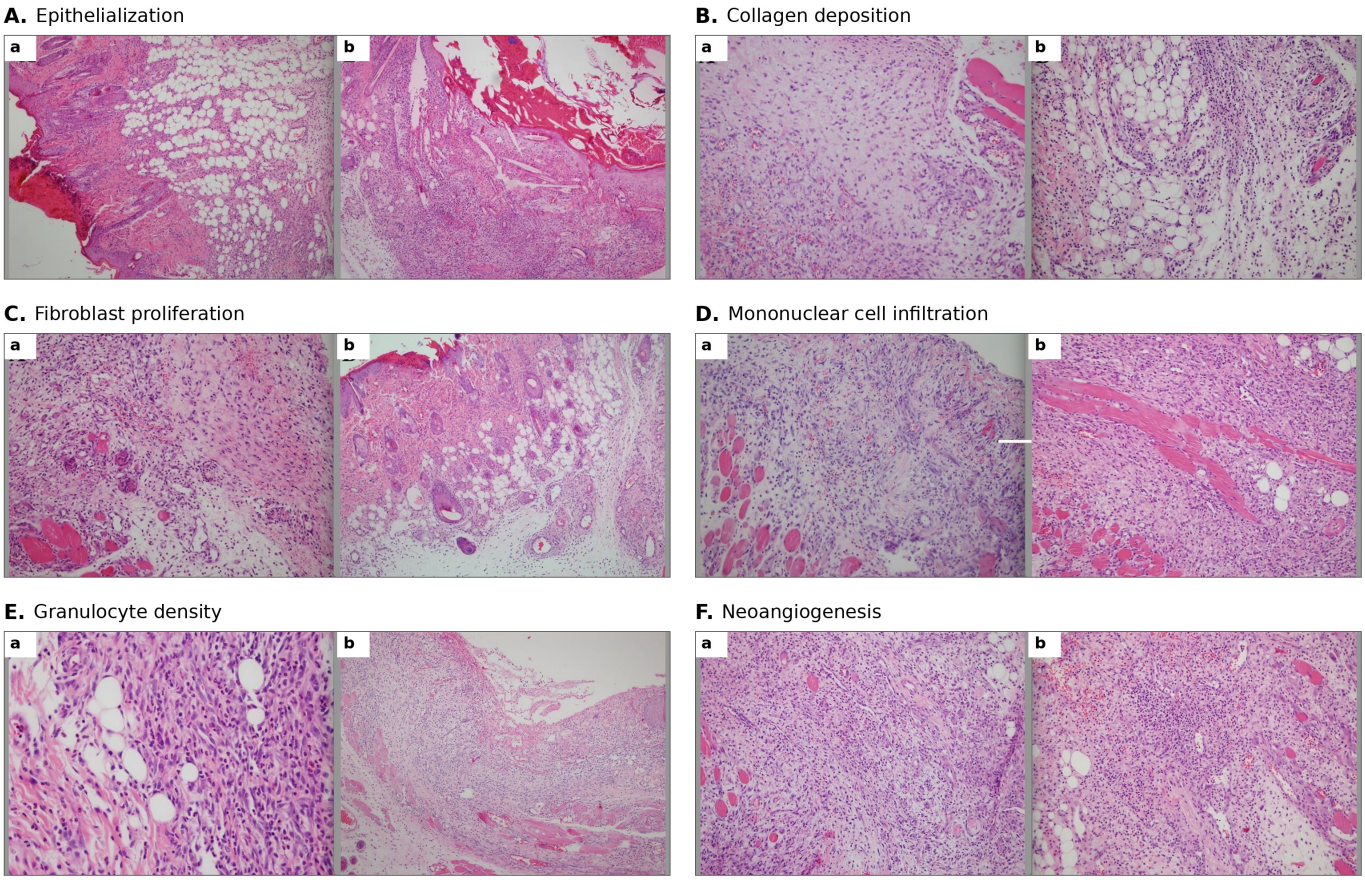

Figure 2. Histopathological findings in the experimental groups. A. Epithelialization. (a) Group 2 showing epithelialization; (b) Group 1 showing absence of epithelialization. B. Collagen deposition. (a) Group 4 showing dense collagen deposition; (b) Group 1 showing reduced collagen deposition. C. Fibroblast proliferation. (a) Group 2 showing dense fibroblast proliferation; (b) Group 1 showing minimal fibroblast proliferation. D. Mononuclear cell infiltration. (a) Group 2 showing high mononuclear cell density; (b) Group 1 showing low mononuclear cell density. E. Granulocyte density. (a) Group 4 showing marked granulocytosis; (b) Group 1 showing moderate granulocytosis. F. Neoangiogenesis. (a) Group 3 showing intense neoangiogenesis; (b) Group 1 showing low neoangiogenesis.

membrane in white rabbits. Building on this experimental concept, the present study established a standardized rat model using a controlled hypopharyngeal–cervical esophageal perforation.

Shih-An Liu et al[14] created a PCF model in Sprague–Dawley rats using Vicryl sutures, Prolene sutures, or Vicryl combined with fibrin glue, and monitored healing for 7 days. Prior to the principal experiment, a pilot study was conducted on 3 rats utilizing the identical incision-and-suture methodology. Severe cervical edema, purulent discharge, tissue necrosis, and feeding difficulty were observed, and 1 rat died on postoperative day 2. To prevent excessive fistula flow and nutritional deficiency, the experimental model was therefore modified by creating a controlled perforation between the hypopharynx and cervical esophagus using a 2.10-mm catheter, which allowed a standardized and reproducible PCF model. In accordance with the literature, the rats were monitored for 7 days and then sacrificed. A meta-analysis of human studies reported no significant difference in PCF-related outcomes between early (≤3 days) and delayed (≥7 days) oral feeding after total laryngectomy. In the present animal model, feeding was initiated on the first postoperative day without restriction to prevent nutritional deterioration during the follow-up period.[15]

Eryılmaz et al[16] evaluated PRP, fibrin tissue adhesive, albumin–glutaraldehyde protein-based adhesive, and synthetic tissue adhesive in a rat PCF model, with an additional control group. In their study, no significant macroscopic difference in fistula formation was observed among the groups, whereas inflammatory cell density and fibroblast density differed histopathologically. However, collagen deposition and neoangiogenesis did not show significant intergroup differences. In contrast, the present study showed a lower frequency of fistula formation, particularly in the PRP group, together with higher collagen deposition in the treatment groups and more prominent neoangiogenesis in the PGE1 and dexpanthenol groups.

Pamuk et al[10] evaluated the effects of *Myroxylon pereirae*, phenytoin and clinoptilolite on wound healing in a PCF model established in rats. The study reported that fistula development was 90% in the control group, 18% in the *Myroxylon pereirae* group, and 27% in the phenytoin group; it was demonstrated that fibroblast proliferation and collagen deposition increased in the *Myroxylon pereirae* group, whereas inflammation scores decreased in the phenytoin group. Clinoptilolite did not provide a significant healing benefit. These findings are consistent with the present study as they highlight the importance of reducing inflammation, increasing fibroblast activity, and promoting collagen deposition in

the healing of PCF. Furthermore, in the present study, macroscopic fistula formation was reduced, particularly in the PRP group, whereas histopathological healing parameters were positively affected in the PRP, PGE1, and dexpanthenol groups.

Eid et al[17] stated that platelet-rich fibrin used after closing the pharynx in patients who have had a total laryngectomy speeds up healing and lowers the risk of fistulas. Although PRF and PRP are distinct platelet-derived products with different preparation methods and biological properties, both contain platelet-related growth factors that may support tissue repair. Consistent with these findings, PRP demonstrated the most consistent improvement across both macroscopic and histopathological parameters.

Prostaglandin E1 analogues promote neoangiogenesis and tissue healing,[18] while dexpanthenol boosts collagen synthesis and fibroblastic activity[19,20] in experimental gastrointestinal investigations. Clinical data suggest reduced complications with postoperative PGE1 use after laryngeal surgery.[21] Therefore, the findings of the present experimental study may provide a rationale for future clinical trials evaluating these agents as adjunctive therapies in patients undergoing laryngectomy or other high-risk head and neck procedures. In this study, all 3 agents improved histopathological healing markers; however, PRP and dexpanthenol may be more practical options given the cost, availability, and short half-life of PGE1.

Previous rat PCF studies reported increased collagen production with recombinant growth hormone and increased fibroblast density with bacterial cellulose.[22,23] In the present study, collagen deposition increased in all treatment groups, whereas fibroblast proliferation was significantly higher in PRP and PGE1 groups.

This study is limited by its experimental animal design, which may not fully reflect the complexity of clinical PCF in humans. Although platelet concentration was not quantified, the standardized double-centrifugation protocol used in this study has been widely employed in experimental PRP studies and has been shown to produce platelet enrichment sufficient for biological activity.[9] The relatively small sample size and short follow-up period precluded evaluation of long-term outcomes. Histopathological assessment was semi-quantitative, and functional parameters such as salivary leakage were not assessed. Therefore, the findings should be interpreted cautiously and require confirmation in further standardized experimental and clinical studies.

This study established a standardized and reproducible experimental PCF model, enabling controlled comparison of treatment modalities under identical surgical and postoperative conditions. Both macroscopic and histopathological parameters were evaluated, and blinded assessment enhanced internal validity. Furthermore, 3 agents with distinct mechanisms of action were investigated within the same experimental framework, allowing direct comparison. In addition to overall intergroup comparisons, pairwise analyses were performed to further explore differences between treatment groups, as also reported in recent experimental PCF studies.

In conclusion, this study comparatively evaluated the effects of PRP, PGE1, and dexpanthenol on wound healing in an experimental PCF model. To the best of the authors' knowledge, this is the first study to compare these 3 agents within the same experimental PCF framework. Platelet-rich plasma demonstrated the most consistent improvement in both macroscopic and histopathological healing parameters, whereas PGE1 and dexpanthenol also enhanced collagen deposition and neoangiogenesis. Therefore, PRP may represent a promising adjunctive approach for improving wound healing and potentially reducing the risk of PCF in clinical practice. Further experimental and clinical studies are required to clarify the underlying mechanisms and to determine the long-term clinical effects of these findings.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Artificial Intelligence Usage Statement: ChatGPT (OpenAI) was used solely to improve the English language, grammar, and readability of the manuscript. All AI-assisted revisions were critically reviewed and approved by the authors. The tool was not used for data analysis, interpretation of the findings, or generation of scientific results.

Ethics Committee Approval: Ethical committee approval was received from the Gülhane Animal Experiments Ethics Committee, University of Health Sciences (Approval No.: ETLIK-2023/23; Date: October 31, 2023).

Peer-review: Externally peer-reviewed.

Acknowledgments: The authors would like to thank Veterinarian Okan Ali Aksoy and Berk Alp Göksel for their scientific consultancy contributions to the study design, methodological development, and interpretation of the findings.

Author Contributions: Conceptualization – A.A.Ö., C.K.; Data curation – A.A.Ö.; Formal analysis – A.A.Ö.; Funding acquisition – Not applicable; Investigation – A.A.Ö., F.T., B.B.B., G.B.D.; Methodology – A.A.Ö., T.T., C.K.; Project administration – A.A.Ö., C.K.; Resources – T.T., C.K.; Software – A.A.Ö.; Supervision – C.K.; Validation – C.K., G.B.D.; Visualization – A.A.Ö., G.B.D.; Writing – original draft – A.A.Ö.; Writing – review & editing – A.A.Ö., T.T., C.K., F.T., B.B.B., G.B.D.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declare that this study received no financial support.

References

1. Mäkitie AA, Irish J, Gullane PJ. Pharyngocutaneous fistula. *Curr Opin Otolaryngol Head Neck Surg*. 2003;11(2):78-84. [CrossRef]
2. Busoni M, Deganello A, Gallo O. Pharyngocutaneous fistula following total laryngectomy: analysis of risk factors, prognosis and treatment modalities. *Acta Otorhinolaryngol Ital*. 2015;35(6):400-405. [CrossRef]
3. Rao KN, Arora RD, Singh A, Nagarkar NM, Aggarwal A. Pharyngocutaneous fistula following primary total laryngectomy: a meta-analysis. *Indian J Surg Oncol*. 2022;13(4):797-808. [CrossRef]
4. Nurden AT. Platelets, inflammation and tissue regeneration. *Thromb Haemost*. 2011;105(suppl 1):S13-S33. [CrossRef]
5. Liu Y, Kalén A, Risto O, Wahlström O. Fibroblast proliferation due to exposure to a platelet concentrate in vitro is pH dependent. *Wound Repair Regen*. 2002;10(5):336-340. [CrossRef]

6. de Perrot M, Fischer S, Liu M, et al. Prostaglandin E1 protects lung transplants from ischemia-reperfusion injury: a shift from pro- to anti-inflammatory cytokines. *Transplantation*. 2001;72(9):1505-1512. [CrossRef]
7. Censabella S, Claes S, Orlandini M, Braekers R, Thijs H, Bulens P. Retrospective study of radiotherapy-induced skin reactions in breast cancer patients: reduced incidence of moist desquamation with a hydroactive colloid gel versus dexpanthenol. *Eur J Oncol Nurs*. 2014;18(5):499-504. [CrossRef]
8. Ebner F, Heller A, Rippke F, Tausch I. Topical use of dexpanthenol in skin disorders. *Am J Clin Dermatol*. 2002;3(6):427-433. [CrossRef]
9. Shin HS, Woo HM, Kang BJ. Optimisation of a double-centrifugation method for preparation of canine platelet-rich plasma. *BMC Vet Res*. 2017;13(1):198. [CrossRef]
10. Pamuk E, Dogan E, Kurtulan O, Güler Tezel YG, Yiğit AA. Effects of Myroxylon pereirae, phenytoin, and clinoptilolite after pharyngocutaneous fistula: an Experimental Animal Model. *Otolaryngol Head Neck Surg*. 2025;172(5):1656-1663. [CrossRef]
11. Hasan Z, Dwivedi RC, Gunaratne DA, Virk SA, Palme CE, Riffat F. Systematic review and meta-analysis of the complications of salvage total laryngectomy. *Eur J Surg Oncol*. 2017;43(1):42-51. [CrossRef]
12. Esteban F, Delgado-Rodríguez M, Mochón A, Solano J, Soldado L, Solanellas J. Hospital stay after total laryngectomy: multivariable retrospective analysis. *Acta Otorrinolaringol Esp*. 2006;57(4):176-182. [CrossRef]
13. Weiss LS, Miller RH, Bates ML, Fisher E, Weiner N, Shepard D. An animal model for pharyngocutaneous fistulas. *Otolaryngol Head Neck Surg*. 1993;108(6):738-742. [CrossRef]
14. Liu SA, Tung KC, Cheng CC, Chiu YT. The impact of different closure materials on pharyngeal wound healing: an experimental animal study. *Eur Arch Otorhinolaryngol*. 2008;265(2):227-231. [CrossRef]
15. Yi X, Hu C, Peng Y, et al. Meta-analysis on the safety and efficacy of early oral feeding after total laryngectomy. *J BUON*. 2021;26(5):2019-2025.
16. Eryılmaz A, Demirci B, Gunel C, et al. Can tissue adhesives and platelet-rich plasma prevent pharyngocutaneous fistula formation? *Auris Nasus Larynx*. 2016;43(1):62-67. [CrossRef]
17. Eid AM, Ebada HA, El-Fattah AMA, Tawfik A. Platelet-rich fibrin: an autologous biomaterial for healing assistance of pharyngeal repair in total laryngectomy. *Eur Arch Otorhinolaryngol*. 2021;278(2):463-470. [CrossRef]
18. Vasiliadis K, Kanellos I, Tsachalis T, et al. Influence of iloprost on healing of colonic anastomosis in rats. *Minerva Chir*. 2007;62(4):241-248.
19. Pehlivanlı F, Aydın O, Karaca G, et al. Healing of ischemic colon anastomosis in rats could be provided by administering dexpanthenol or coenzyme Q10. *J Clin Med*. 2018;7(7):161. [CrossRef]
20. Ermutlu C, Erkılıç E, Kılıç E, et al. Effect of dexpanthenol on colonic anastomosis healing in rats. *Med Weter*. 2021;74(10):6135-2021. [CrossRef]
21. Shiga K, Tateda M, Saijo S. Complication-free laryngeal surgery after irradiation failure with prostaglandin E1 administration. *Ann Otol Rhinol Laryngol*. 2002;111(9):783-788. [CrossRef]
22. Kucuk N, Sarı M, Midi A, Yumusakhuylu AC, Findik O, Binnetoglu A. Effectiveness of Recombinant human growth hormone for pharyngocutaneous fistula closure. *Clin Exp Otorhinolaryngol*. 2015;8(4):390-395. [CrossRef]
23. Demir B, Sarı M, Binnetoglu A, et al. Comparison of pharyngocutaneous fistula closure with and without bacterial cellulose in a rat model. *Auris Nasus Larynx*. 2018;45(2):301-305. [CrossRef]