



(REVIEW ARTICLE)



## Gene therapy and stem cells in cochlear regeneration: A Comprehensive Review

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International Journal of Science and Research Archive, 2025, 16(02), 924-925

Publication history: Received on 09 July 2025; revised on 16 August 2025; accepted on 18 August 2025

Article DOI: <https://doi.org/10.30574/ijrsra.2025.16.2.2404>

### Abstract

Sensorineural hearing loss (SNHL) remains a significant clinical challenge due to the limited regenerative capacity of cochlear cells in mammals. Recent advancements in gene therapy and stem cell technologies offer promising avenues for cochlear regeneration. This review synthesizes current research on the application of gene therapy and stem cells in cochlear regeneration, focusing on their mechanisms, therapeutic potentials, and clinical implications. We explore the roles of various stem cell types, including mesenchymal stem cells (MSCs) and induced pluripotent stem cells (iPSCs), and discuss gene editing strategies aimed at restoring cochlear function. The review also addresses the challenges and future directions in this field, emphasizing the need for further research to translate these therapies into clinical practice.

**Keywords:** Cochlea; Gene Therapy; Stem Cells; Cochlear Regeneration; Sensorineural Hearing Loss

### 1. Introduction

Abdominal emergencies appendicitis, acute cholecystitis, and intestinal perforations remain frequent causes of urgent surgery and important determinants of morbidity and mortality when diagnosis or treatment is delayed. In the last five years, there has been intense debate over conservative versus operative management, optimization of surgical timing, and selection of strategies for high-risk patients. International and national reviews and guidelines have updated recommendations on indications for antibiotic therapy, timing for surgical intervention, and source control techniques. This article synthesizes the main evidence (08/2020–08/2025) to guide emergency and urgent care practices (FERREIRA, M. et al. Advances in urgent abdominal surgery. *Annals of Medicine and Surgery*, v. 81, p. 104-118, 2022.).

### 2. Methodology

A narrative review was conducted in the following stages

(1) searches in PubMed/PMC, SciELO, and guideline repositories between 08/2020 and 08/2025 using the terms “acute appendicitis management,” “nonoperative management appendicitis randomized trial,” “acute cholecystitis Tokyo Guidelines,” “early vs delayed cholecystectomy,” “intestinal perforation peritonitis management,” and their equivalents in Portuguese; (2) selection of high-quality documents (guidelines, systematic reviews, meta-analyses, relevant RCTs, and national reviews); (3) extraction of recommendations on diagnosis, surgical indication, antibiotic therapy, surgical techniques (laparoscopic vs. open), source control, and septic patient management; and (4) critical synthesis of the evidence.

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### 3. Discussion and Results

#### 3.1. Acute Appendicitis

Laparoscopic appendectomy is now considered the gold standard for most patients, providing reduced postoperative pain, shorter recovery times, and fewer wound complications. Recent studies emphasize the safety of early discharge protocols, even within 24 hours after surgery, for selected patients. Additionally, conservative management with antibiotics may be appropriate for non-complicated appendicitis in carefully selected cases, but recurrence risk remains a concern. (SANTOS, V. et al. Laparoscopic appendectomy and early discharge: a safe approach. *Surgical Endoscopy*, v. 36, p. 567-574, 2022.)

#### 3.2. Acute Cholecystitis

Early laparoscopic cholecystectomy within the first 72 hours is now the preferred approach, reducing complication rates and hospital costs. The use of Tokyo Guidelines 2018 for severity grading helps tailor treatment strategies, with percutaneous cholecystostomy reserved for critically ill patients who are poor surgical candidates. Advances in imaging, such as contrast-enhanced ultrasound, have improved diagnostic accuracy. (MARTINS, A. et al. Early cholecystectomy versus delayed approach. *HPB*, v. 24, p. 905-912, 2022.)

#### 3.3. Intestinal Perforations

The management of intestinal perforations depends on etiology, location, and patient stability. Surgical repair, either via open or laparoscopic approach, remains the cornerstone. Damage control surgery is essential for unstable patients, with staged reconstruction after physiological stabilization. Enhanced recovery protocols, including early nutrition, have been shown to reduce morbidity. (COSTA, F. et al. Surgical strategies for intestinal perforation. *Journal of Trauma and Acute Care Surgery*, v. 92, p. 44-53, 2022.)

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### 4. Conclusion

The past five years have brought significant refinements to the emergency surgical management of appendicitis, cholecystitis, and intestinal perforations. While surgical intervention remains the mainstay in most cases, nonoperative strategies particularly for uncomplicated appendicitis and inoperable cholecystitis are supported by robust evidence when applied to carefully selected patients. Early source control, minimally invasive techniques, and individualized treatment pathways based on validated severity scoring systems form the cornerstone of modern practice.

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### Compliance with ethical standards

#### *Disclosure of conflict of interest*

No conflict-of-interest to be disclosed.

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