



## IJCR Global Summit 2025 Book of Abstracts

### A Word from the Organizers

Welcome to the Official Book of Abstracts for the 2025 IJCR Global Summit.

We are proud to present this collection of scientific works, which formed the intellectual core of our 2025 Summit. Hosted on August 23–24 at the Faculdade de Medicina da Universidade de São Paulo (FMUSP), recognized as the premier medical institution in Brazil and Latin America and as a global leader in healthcare, this event gathered the brightest minds in the field. This volume serves as both a historical record and a testament to the innovation driving clinical research forward.

The caliber of this year's submissions was truly exceptional. We are pleased to feature 14 abstracts that demonstrate an impeccable standard of research. The diversity of topics reflects our global community and the complex challenges we address together. Engagement during the sessions was equally remarkable, with our jury providing actionable feedback that sparked high-level scientific debate.

As you explore these works, you will witness the convergence of discipline, creativity, and rigor. We extend our gratitude to every author; your contributions ensure the IJCR Global Summit remains a beacon of excellence.

We hope this collection inspires your future endeavors and fosters new collaborations in the year ahead.

*Note: Please note that these abstracts appear in their original submission format and have not undergone copyediting, editorial or peer review.*

Sincerely,

**The 2025 IJCR Global Summit Conference Directors**

**Dr. Mariana Flaifel**

**Dr. Peter Samuel**

**Dr. Heba Sati**

*And Dr. Gregory Nicolas, Chief Executive Officer*

# Efficacy and Safety of Tapinarof for Atopic Dermatitis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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**Introduction and Objective:** Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterized by severe pruritus and eczematous lesions, negatively impacting patient quality of life. Current topical treatments like corticosteroids, have notable limitations regarding long-term safety and patient adherence. This meta-analysis evaluates the efficacy and safety of Tapinarof cream, a novel topical aryl hydrocarbon receptor modulating agent, in both adult and pediatric populations with mild-to-severe AD.

**Methods:** We performed a systematic review and meta-analysis of placebo-controlled, randomized trials of Tapinarof cream 1% once daily (QD) in patients with mild-to-severe AD. PubMed, Embase, Cochrane, ClinicalTrials.gov, and grey literature sources were searched for trials published up to March 2025. Data were extracted from published reports, and quality assessment was performed per Cochrane recommendations. Risk Ratios (RRs) with 95% confidence intervals (CIs) were pooled across trials. The primary endpoints of interest were Investigator Global Assessment (IGA) success, Eczema Area and Severity Index-75% (EASI75) response, improvement in Peak Pruritus Numeric Rating Scale (PP-NRS) scores, and incidence of adverse events.

**Results and Discussion:** Out of 96 database records, 5 randomized trials and 1191 patients were included. Compared to placebo, Tapinarof 1% QD was associated with significantly greater IGA success (RR = 3.03, 95% CI: 1.94–4.74, P = 0.002), achievement of EASI75 response (RR = 2.99, 95% CI: 1.94–4.60, P = 0.002), and clinically meaningful improvement in PP-NRS scores of  $\geq 4$  points (RR = 1.58, 95% CI: 1.10–2.26, P = 0.002). Regarding safety, treatment with Tapinarof 1% QD showed a statistically significant increase in the overall incidence of adverse events compared to placebo (RR = 1.39, 95% CI: 1.02–1.90, P = 0.04). No significant difference was observed in serious adverse events (RR = 1.98, 95% CI: 0.36–24.69, P = 0.31).

**Conclusion:** The findings suggest that Tapinarof cream demonstrates significant efficacy in treating mild-to-severe AD, providing substantial improvement in clinical signs and symptoms and meaningful reduction in pruritus. Tapinarof was generally well-tolerated, supporting its clinical utility as a non-steroidal topical treatment for AD.

## **Analysis of the Change in the Epidemiological Profile of Deaths from Ischemic Stroke in Brazil from 2014 to 2023**

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**Introduction and Objective:** Ischemic stroke (IS) is a leading cause of death in Brazil, resulting from the interruption of blood flow to the cerebral arteries. It is estimated that 90% of cases can be prevented by controlling ten risk factors. Despite advances in prevention and treatment, stroke remains highly prevalent in the country, with a significant increase in causes of death between 2014 and 2023. Analyzing hospital care conditions is essential to guide public policies and optimize the allocation of resources within the Sistema Único de Saúde (SUS), since appropriate management includes controlling comorbidities, preventing complications, and functional rehabilitation. This study aims to identify the structural deficiencies in Brazilian hospitals that contribute to the high incidence of ischemic stroke and the consequent increase in deaths in recent years.

**Methods:** Epidemiological, descriptive, and cross-sectional study. Data collection was carried out through the DATASUS (TABNET) health information bank, corresponding to deaths from cerebral infarction in Brazil in the years 2013 and 2024. The variables used are: race/color, sex, and age group.

**Result and Discussion:** In our study, it was observed that, from 2014 to 2023, 16,930 deaths from ischemic stroke were recorded, with a significant increase from 4,294 cases in 2014 to 12,636 cases in 2023, a growth of 194%. We analyzed an equality of male and female sexes, in which an increase in cases was observed from 60 years of age and a predominance of the white race, representing 62% of cases. Regarding the findings, we noted a large increase in deaths, which are worrying as these increases occur each year.

**Conclusion:** Finally, this epidemiological study's main objective was to demonstrate an exponential increase in deaths from ischemic stroke in Brazil between 2014 and 2023. This analysis revealed a threefold increase in deaths compared to previous years, with a higher incidence among individuals over 60 years of age and white people. This rise in cases highlights the need for greater public policy and information, as well as population-based studies to understand the cause of this increase in deaths from a disease that already has effective treatments.

# Temporal Trend in Ovarian Cancer Mortality in Brazil between 2010 and 2023: An Ecological Time-Series Study

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**Introduction and Objectives:** Ovarian cancer is among the leading causes of death from gynecological neoplasms worldwide. Due to non-specific symptoms and the absence of effective screening strategies, most diagnoses occur at advanced stages, resulting in low survival rates. In Brazil, evaluating mortality trends is essential to assess the effectiveness of public health policies and guide strategies for early diagnosis and timely treatment. This study aims to analyze the temporal trend of ovarian cancer mortality in Brazil from 2010 to 2023, including national and regional perspectives.

**Methodology:** This is an ecological time-series study using data extracted from the Mortality Information System (SIM) via the DATASUS platform. All female deaths registered under ICD-10 code C56 (malignant neoplasm of the ovary) from 2010 to 2023 were included. Mortality rates were age-standardized according to the World Health Organization (WHO) standard population. The Joinpoint Regression Program (version 4.9.1.0) was used to calculate the Annual Percent Change (APC) and Average Annual Percent Change (AAPC), with a 95% confidence interval and a 5% significance level.

**Results and Discussion:** Between 2010 and 2023, ovarian cancer mortality in Brazil showed a stable trend (AAPC: -0.2%; 95% CI: -0.6 to 0.3;  $p > 0.05$ ). There was a slight increase from 2010 to 2014 (APC:+0.5%), a decrease from 2015 to 2019 (APC: -0.8%), and stabilization until 2023. The Southeast maintained the highest mortality rates throughout, while the North and Northeast regions showed slight increases. These findings suggest stagnation in the effectiveness of early detection policies and highlight persistent regional disparities. While more developed regions may benefit from better infrastructure and access to care, underserved areas face barriers that delay diagnosis and treatment. The absence of a consistent downward trend in national mortality rates indicates limited progress in controlling the disease. Strengthening cancer care networks, investing in health education, and implementing targeted policies, especially in high-risk regions, are necessary to reduce inequalities and improve outcomes.

**Conclusion:** The persistent stability in ovarian cancer mortality in Brazil underscores the urgent need to expand early detection programs, ensure equitable access to oncological care, and prioritize regional interventions to reduce disparities and enhance women's survival rates across the country.

## The Use of Ablative Laser Therapy in Lichen Sclerosus et Atrophicus of the Vulva: A Systematic Review and Meta-Analysis

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**Introduction & Objectives:** Lichen sclerosus et atrophicus (LSA) is a chronic inflammatory condition primarily affecting the genital and perianal areas, with occasional extragenital involvement. Treatment typically involves high to mid-potency topical corticosteroids, which are effective for both genital and extragenital lesions. Ablative laser treatment has emerged as a promising modality. This study aims to assess its efficacy and safety in treating LSA.

**Materials & Methods:** A systematic search of PubMed was conducted using the terms: ‘vulvar lichen sclerosus’ AND ‘ablative laser’ OR ‘fractional CO<sub>2</sub> laser’ OR ‘Er:YAG laser’. Eligible studies were randomized controlled trials evaluating fractional ablative laser in adult women with confirmed LSA. Two primary outcomes were analyzed: change in subjective total symptom burden, assessed using visual analog scale (VAS) scores, and objective disease severity, including physician-rated scoring systems (Lesion Severity [LS] Score, Clinical Scoring System, and vulvar appearance VAS) that assessed features such as atrophy, fissures, and hyperkeratosis. VAS total was computed from domains such as itching, burning, and pain, and analyzed as a mean difference (MD). Severity scores were pooled using standardized mean difference (SMD). MD and SMD were pooled using a DerSimonian–Laird random-effects model. Heterogeneity was assessed using I<sup>2</sup>. Risk of bias was evaluated with the Cochrane RoB 2.0 tool. This meta-analysis followed PRISMA guidelines.

**Results:** Four randomized controlled trials comprising a total of 172 patients were included in the meta-analysis. Three studies evaluated ablative fractional CO<sub>2</sub> laser therapy, while one study evaluated Nd:YAG + Er:YAG dual laser. Comparator arms included sham laser, topical clobetasol propionate 0.05% or low-dose CO<sub>2</sub> laser acting as a functional placebo. The number of laser treatment sessions ranged from three to five, and follow-up periods spanned from 6 to 48 weeks. Ablative laser therapy showed a non-significant reduction in VAS total compared to controls with a MD of -0.51 (95% CI -1.60 to 0.59; p = 0.37; I<sup>2</sup> = 64%). Similarly, a pooled analysis of LS severity scores showed a non-significant reduction with a SMD of -0.26 (95% CI -0.69 to 0.17; p = 0.24; I<sup>2</sup> = 50%). Ablative laser therapy was consistently well-tolerated, with no serious adverse events reported.

**Conclusion:** In conclusion, this meta-analysis has shown no significant overall improvement in symptoms burden or disease severity in patients with LSA treated with ablative laser therapy in comparison with controls. Corticosteroid therapy remains the mainstay, and laser therapy can be added as an adjunct. Further large-scale trials are needed to establish its role in LSA.

# Cranial Vault Expansion Techniques for Syndromic Craniosynostosis: A Systematic Review of Intracranial Pressure and Neurocognitive Outcomes

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**Introduction and Objectives:** Syndromic craniosynostosis, particularly in Apert and Crouzon syndromes, often leads to intracranial hypertension (ICH) and neurocognitive impairment. Early surgical intervention is necessary to reduce complications from premature suture fusion, but the optimal initial cranial vault expansion technique remains controversial. This systematic review evaluates and compares neurocognitive and intracranial pressure outcomes following different primary surgical strategies in treatment-naïve pediatric patients with syndromic craniosynostosis.

**Methods:** A systematic search of PubMed, Embase, and SciELO databases identified 780 articles. Following duplicate removal, six reviewers independently screened titles and abstracts using the Rayyan platform, resulting in the full-text review and final inclusion of 10 comparative studies. Inclusion criteria required studies to compare outcomes between posterior vault distraction osteogenesis (PVDO) and open cranial vault remodeling in patients with Apert or Crouzon syndromes. Key data extracted included objective markers of ICH (e.g., tonsillar herniation, papilledema) and results from standardized neurocognitive assessments (e.g., Bayley Scales of Infant Development, PedsQL).

**Results and Discussion:** Our analysis indicates that primary posterior cranial vault expansion, particularly PVDO, is effective for cranial decompression and is associated with a reduced need for subsequent craniofacial surgeries. For ICH management, posterior expansion was more effective than frontal approaches in resolving cerebellar tonsillar herniation. In contrast, the effect on neurocognition was less clear. Although surgery is vital for normalizing intracranial dynamics, we found no significant differences in neurodevelopmental outcomes between the surgical techniques. Notably, cognitive scores in syndromic cohorts remained consistently below those of non-syndromic peers, highlighting the significant impact of the underlying genetic diagnosis on neurodevelopment.

**Conclusion:** Primary posterior cranial vault expansion is an effective initial strategy for managing ICH in syndromic craniosynostosis and may decrease the long-term surgical burden. However, a significant limitation in the current literature is the lack of direct, high-quality comparative trials. This evidence gap makes it difficult to establish definitive clinical guidelines. Therefore, prospective, multicenter studies with standardized outcome measures are needed to determine the optimal surgical approach for this complex patient population, with the goal of improving both structural and functional outcomes.

## Accuracy of Liquid Biopsy with cfDNA from Cerebrospinal Fluid for Detection of the H3K27 M Mutation in Pediatric Diffuse Midline Gliomas: A Diagnostic Meta-Analysis

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**Introduction and Objectives:** Diffuse midline gliomas (DMG) are aggressive tumors associated with the H3K27M mutation, with a poor prognosis (SOLOMON et al., 2016). Due to the limitations of tissue biopsy (LOUIS et al., 2021), associated with the risks inherent to the surgical technique, liquid biopsy with cfDNA/ctDNA through cerebrospinal fluid (CSF) emerges as a viable alternative for diagnosis and monitoring (Li et al., 2021). This study evaluates its accuracy for detecting the H3K27M mutation in pediatric DMG, with tissue biopsy as the gold standard.

**Methodology:** This study is a systematic review with meta-analysis. The search in the PubMed, Embase, and Web of Science databases used the terms “Glioma,” “Liquid Biopsy,” “Pediatrics,” and “whole genome sequencing” with synonyms and Boolean operators “AND” and “OR.” Following PRISMA 2020, observational studies that evaluated the accuracy of liquid biopsy with cfDNA/ctDNA obtained from CSF for detecting the H3K27M mutation in children and adolescents with DMG were included. Statistical analyses were performed in R (v.4.4.3), using the ‘meta’ and ‘meda’ packages.

**Results and Discussion:** Six observational studies were included, totaling 140 paired samples of CSF and tumor tissue. The SROC curve showed an AUC of 0.86, indicating high accuracy, with the Rutter-Gatsonis model. The pooled specificity was 69.3%, PLR was 2.88, and NLR was 0.17. Six studies (n = 108 paired samples) evaluated sensitivity, with values ranging from 75% to 100%. The pooled sensitivity was 94% [95% CI: 87%–97%], with no significant heterogeneity ( $I^2 = 0\%$ ;  $\tau^2 = 0$ ;  $p = 0.5144$ ), confirming high diagnostic accuracy. Four studies (n = 32 negative cases) evaluated specificity, with a range of 0% to 100%. The pooled specificity was 59% [95% CI: 16%–92%], with no heterogeneity ( $I^2 = 0\%$ ;  $\tau^2 = 2.79$ ;  $p = 0.9335$ ), suggesting a limitation for diagnostic exclusion, influenced by analytical noise and small sample sizes.

**Conclusion:** Liquid biopsy with cfDNA/ctDNA from CSF demonstrated moderate specificity, high sensitivity, and high accuracy for detecting the H3K27M mutation in pediatric GMD, representing a viable minimally invasive alternative to tissue biopsy in hard-to-access settings. These findings support its incorporation as a potential molecular screening tool for diagnostic protocols.

## Prognosis of intracranial meningiomas with TERTp mutation: systematic review with meta-analysis

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**Introduction and Objectives:** Intracranial meningiomas are the most common primary neoplasms in adults, being extra-axial tumors originating from the arachnoid cells of the leptomeninges (LYNES, J. et al., 2022). TERTp mutations (C228T/C250T) activate telomerase and define aggressive and recurrent tumors, differing from wild-type tumors (SPIEGL-KREINECKER, S. et al., 2018). Although recognized by WHO as a marker of aggressiveness, its impact on survival and recurrence remains poorly defined. This meta-analysis evaluated the prognostic impact of TERTp mutations on overall survival (OS), progression-free survival (PFS), and recurrence. **METHODOLOGY:** This study is a systematic review with meta-analysis. The search in the PubMed, Embase, and Web of Science databases used the terms “Meningioma,” “TERT Promoter,” and “Prognosis” with synonyms and Boolean operators ‘AND’ and ‘OR.’ Following PRISMA 2020, cohorts comparing mutated TERTp vs. wild type were included, with OS, PFS, and recurrence results. Bias was assessed by funnel plot and Egger’s test. Analyses were performed in R (v.4.4.3), “meta” package.

**Results and Discussion:** The meta-analysis revealed a strong association between TERT promoter mutations (TERTp) and worse prognosis in intracranial meningiomas. For OS, five studies (n = 1155) showed a significantly higher risk of death in tumors with TERTp mutation compared to the wild type (HR = 5.24; 95% CI: 1.77–15.53; p = 0.003), with high heterogeneity (I<sup>2</sup> = 86.2%). The mean difference in OS confirmed the finding, with a 43.9-month reduction in survival for tumors with TERTp mutation (95% CI: -52.6 to -35.2; p < 0.001; I<sup>2</sup> = 91.6%). For PFS, four studies (n = 1,243) indicated a significantly higher risk of progression in patients with TERTp mutation (HR = 10.83; 95% CI: 7.43–15.76; p < 0.001), with high consistency (I<sup>2</sup> = 0%). The mean difference in PFS indicated progression 28.9 months earlier in this group (95% CI: -37.0 to -20.8; p < 0.001), with moderate heterogeneity (I<sup>2</sup> = 47.1%).

**Conclusion:** These data indicate a direct impact on prognostic stratification, cautious oncological follow-up with early adjuvant indication (Wang et al., 2024). Meningiomas with TERTp mutation have poor prognosis, with reduced OS and shorter PFS. Their presence increases the risk of death by over five times and recurrence by ten times compared to wild-type TERTp. This supports TERTp mutation as a molecular marker for risk stratification, with potential use in diagnostics and personalized therapy, especially in WHO grade 2 meningiomas.

## Abdominal Wall Reconstruction Techniques: Literature Review and Algorithm Proposal

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**Introduction and Objectives:** The abdominal wall plays a vital role in visceral protection, postural stabilization, and the maintenance of intra-abdominal pressure. The loss of integrity of this structure leads to the impairment of these functions, with incisional hernia being the main representative among possible associated defects, in addition to large oncological resections, trauma, and tissue loss due to infection<sup>1,2,3</sup>. Plastic Surgery plays a central role in abdominal wall reconstructions. The choice of the ideal technique requires evaluation by an experienced team, considering the characteristics of the defect, the patient's clinical conditions, and the resources available at the service. The aim of this study is to briefly review the anatomy of the abdominal wall. Analyze the main challenges and difficulties encountered by surgeons when faced with the need to reconstruct an abdominal wall, considering the anatomical, technical-surgical aspects, and the conditions of the patient and the medical service. Review the main techniques for abdominal wall reconstruction. In addition, propose an algorithm for abdominal wall reconstruction based on the experience of a Brazilian reference service.

**Methods:** Literature review in the PubMed, SciELO, and EMBASE databases. The descriptors “abdominal wall reconstruction,” “abdominal wall anatomy,” “myocutaneous flap,” and “surgical flaps” were used. Studies published from 2018 onwards were selected. Construction of an algorithm based on the literature review conducted, as well as on the experience of the national reference institution.

**Results:** The decision regarding the definitive closure technique depends on the origin, location, size of the defect, and clinical conditions related to the patient. Complex wounds that are not suitable for primary closure in patients who cannot tolerate reconstruction in a first moment are candidates for negative pressure therapy. A meta-analysis published in 2024 showed that negative pressure therapy in abdominal wounds reduced complication rates at the surgical site, such as infection (RR 0.512,  $p < 0.001$ ) and dehiscence (RR 0.581,  $p < 0.001$ ), as well as hospital stay (average reduction of 2.6 days,  $p < 0.001$ ) and readmission rate (RR 0.565,  $p 0.014$ ). Definitive closure can be performed with local, regional, or free flaps. Local flaps are more conservative options. Regional ones are reserved for larger defects and can be designed as fasciocutaneous, myocutaneous, or muscular flaps covered with skin grafts. Free flaps, in turn, have greater technical complexity but also allow for the coverage of large defects. In the algorithm, we divide the lesions into partial and total depending on the thickness of the defect. Partial defects can be corrected with primary closure, local flaps, and grafts. Total and more complex defects can be reconstructed through techniques such as component separation, grafts, and, most commonly, flaps. The choice of flap depends on the location of the defect (upper and lower), the availability of local tissue, and can be locoregional or microsurgical<sup>8</sup>. The use of dual mesh and the application of botulinum toxin are also tools that can assist the surgeon at the time of abdominal wall reconstruction.

**Conclusion:** Large abdominal wall defects are serious health conditions that are difficult to manage and remain a challenge for plastic surgeons and multidisciplinary teams. In-depth knowledge of anatomy is fundamental to the choice of the technique employed. The advancement of surgical techniques has increased patient safety and the available therapeutic options. The appropriate choice of flap applied to the patient's conditions, and the availability of resources optimizes results and reduces complications.

## Effectiveness of Stromal Vascular Fraction-Enriched Fat Grafting on Facial Skin Quality: A Meta-Analysis of Randomized Controlled Trials

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**Introduction & Objectives:** Stromal vascular fraction (SVF) is used in facial fat grafting to enhance skin rejuvenation, but its clinical efficacy remains under debate. This study aims to evaluate the effect of SVF-enriched autologous fat grafting on facial skin quality, specifically targeting wrinkles and texture, using standardized VISIA imaging data from randomized controlled trials.

**Materials & Methods:** A systematic search across PubMed, Scopus, and Cochrane databases was performed using the following keywords: "stromal vascular fraction" AND "skin quality". Primary outcome of interest included VISIA-based wrinkle and texture scores. Data Effect sizes (Cohen's d) were calculated, and random-effects meta-analysis using the DerSimonian-Laird method was performed. Risk of bias was assessed using the Cochrane RoB 2.0 tool (Table 1). Mean differences (MD) with 95% CI were pooled across trials. This meta-analysis follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

**Results:** Two randomized controlled trials and 78 patients were included in this meta-analysis. Results from Yin et al. (2020) study showed large improvement for SVF treatment groups in VISIA-wrinkle scores (Cohen's d = 1.49) and VISIA-texture scores (Cohen's d = 1.08), while Van Dongen et al. (2021) found a negative effect in SVF treatment groups for both VISIA-wrinkle (Cohen's d = -0.86) and texture scores (Cohen's d = 0.13). A pooled effect size of both studies showed no difference between groups for both VISIA-wrinkle and texture scores (MD 0.29; 95% CI -2.01 to 2.60; p = 0.80; I<sup>2</sup> = 93% and MD 0.57; 95% CI -0.36 to 1.49; p = 0.23; I<sup>2</sup> = 66%, respectively).

**Conclusion:** This meta-analysis highlights discrepancies between studies investigating SVF in fat grafting. Although individual studies showed divergent results, the pooled analysis suggests a modest and statistically non-significant trend favoring SVF-enriched fat grafting for texture improvement, with high heterogeneity and no significant benefit for wrinkle reduction. Current evidence does not support a consistent clinical advantage. Further large-scale, well-controlled trials are warranted.

## Back to the Flow: A Comprehensive Systematic Review and Meta-Analysis of Epinephrine in the Treatment of No-Reflow

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**Introduction:** The no-reflow phenomenon is defined as inadequate microvascular reperfusion despite successful epicardial coronary recanalization and is a serious complication of percutaneous coronary intervention, associated with multiple adverse outcomes, occurring from 11% to 41% in acute coronary syndrome. Its multifactorial pathophysiology includes endothelial injury, distal embolization, and vasospasm. Thus, intracoronary epinephrine has shown promising results due to its  $\beta_2$ -mediated vasodilation and  $\alpha_1$ -driven support of coronary perfusion in hypotensive patients, especially when compared to adenosine. This meta-analysis then synthesizes the available evidence on intracoronary adrenaline for treating no-reflow, focusing on both angiographic and clinical outcomes.

**Methods:** A systematic search was performed in compliance with PRISMA standards across MEDLINE, Scopus, Embase, Cochrane, and Web of Science. We included studies comparing epinephrine with conventional treatment or other drugs. The primary outcome was TIMI flow. Secondary outcomes included major adverse cardiovascular events (MACE), heart failure (HF), mortality, left ventricular ejection fraction (LVEF), and myocardial blush grade.

**Results and Discussion:** Eleven studies met the inclusion criteria, comprising 700 patients in the epinephrine group and 298 in the control group. TIMI flow was analyzed using single-arm meta-analyses by stratifying patients into two subgroups: refractory and primary no-reflow. In the first group ( $n = 226$ ), 63% achieved TIMI 3 flow (95% CI: 0.53–0.72;  $I^2 = 48.7\%$ ), while in the second ( $n = 201$ ), the success rate was higher, at 86% (95% CI: 0.77–0.93;  $I^2 = 51.9\%$ ). For MACE, the pooled proportion reported an incidence of 14% in refractory and 18% in primary no-reflow, while the comparison with conventional treatment revealed a lower risk in epinephrine group (RR 0.45; 95% CI: 0.23–0.87;  $p = 0.01$ ;  $I^2 = 0\%$ ) and, with adenosine, no difference was found (RR 0.94; 95% CI: 0.56–1.58;  $p = 0.49$ ;  $I^2 = 0\%$ ). Considering HF events, the proportion analysis of the conventional group had an incidence of 11% (95% CI: 0.00–0.46;  $I^2 = 84.6\%$ ), and the adenosine group had 5% (95% CI: 0.02–0.09;  $I^2 = 0\%$ ), while no difference was found in comparative analysis.

**Conclusion:** Therefore, Intracoronary epinephrine was associated with favorable outcomes, and the higher success rate in primary no-reflow may reflect earlier intervention and less severe microvascular damage. Its modest advantage over adenosine reinforces therapeutic potential and underscores epinephrine as a safe and potent drug, mainly in refractory no-reflow. These findings, however, call for larger trials to determine the best pharmacologic strategy.

## Analysis of the Effect of Tamoxifen on the Liver Function of Rats Subject to Hepatic Ischemia and Reperfusion

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### Ethical and Funding Considerations

Project approved by the Institutional Ethics Committee (CEUA) under protocol 2105/2024. Scientific initiation project with approved FAPESP grant. Process number 2024/23477-1.

**Introduction and Objectives:** Ischemia and reperfusion (IR) injury is a major cause of primary graft dysfunction (PGD), which can result in irreversible organ failure. Studies suggest that PGD occurs in approximately 5% to 20% of liver transplants due to IR, which also increases the incidence of acute and chronic rejection, increasing the need for retransplantation. Therefore, drugs with anti-inflammatory, antifibrotic, and antiproliferative effects, such as tamoxifen (TAM), may be an interesting strategy to intervene in the progression of the inflammatory and oxidative processes that occur during hepatic IR. Therefore, experimental models that mimic these conditions are extremely important. Therefore, the objective of this study was to analyze the effects of tamoxifen on liver function in animals subjected to an experimental model of ischemia-reperfusion liver injury.

**Materials and Methods:** Twenty-four male Wistar rats, weighing 250 to 300g, were studied and divided into three groups: SHAM Group (n=8) - without IR; IR Group - rats subjected to hepatic ischemia and reperfusion (1 hour of ischemia and 4 hours of reperfusion) (n=8); TAM Group - animals pretreated with tamoxifen and subjected to the IR process. The animals were subjected to partial hepatic ischemia (70%) for 1 hour and a reperfusion period of 4 hours. TAM was administered by gavage at a dose of 10mg/kg in two doses: 24 hours before and 2 hours before hepatic IR. Serum levels of biochemical markers of liver function were evaluated.

**Results:** Animals in the SHAM group showed normal levels of ALT, AST, Gamma GT and Alkaline Phosphatase (271±48 U/L; 203±83 U/L; 2.5±0.7 U/L; 90±10 U/L, respectively). However, while animals in the IR group exhibited an increase in these markers, treatment with TAM significantly reduced their levels (ALT: 6651±1273 U/L vs. 543±44 U/L; AST: 4072±846 U/L vs. 271±100 U/L; Gamma GT: 21±1 U/L vs. 5±0.5 U/L; Alkaline phosphatase 185±5 U/L vs. 90±6 U/L, respectively; p<0.05 comparing all groups).

**Conclusions:** Tamoxifen was effective in protecting the animals' liver function, as demonstrated by the reduction in serum levels of biochemical markers, which were elevated after IR injury

## Bone Reconstruction and Current Advances: Techniques and Translational Basis

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**Introduction and Objectives:** Medical advances in bone trauma, degenerative diseases, and congenital diseases have reduced mortality rates and increased life expectancy. However, less invasive and more effective interventions are needed. Therefore, several options are being studied to stimulate this regeneration and improve clinical outcomes, including bioceramics, natural and synthetic polymers, metals, and using cell sources such as mesenchymal stem cells from bone marrow. This review examines the use of biomaterials and biopolymers for bone tissue engineering and analyzes the current outcomes for bone reconstruction. This review examines the use of biomaterials and biopolymers for bone tissue engineering and analyzes the current outcomes for bone reconstruction.

**Methodology:** This is a narrative review based literature search on PubMed using the terms "tissue engineering", "bone reconstruction", "biomaterials" and "biopolymers". The publication period was between 2020 and 2025, totaling 18 articles available in English.

**Results and Discussion:** Several technologies were analyzed. Bioceramics, such as hydroxyapatite, tricalcium phosphate, and bioglass, mimic the mineral phase of bone, are osteoconductive, and can be used as bone grafts or implants. Natural polymers, such as collagen, gelatin, alginate, chitosan, and hyaluronic acid, can be of animal or plant origin, promote cell adhesion, growth, and differentiation, and have low immunogenicity. Synthetic polymers, such as polyglycolic acid, polyvinyl alcohol, polycaprolactone, and polylactic acid, offer customization, stability, and durability, although they present poor compatibility. Metals such as titanium and cobalt-chromium stand out for their biocompatibility and mechanical and corrosion resistance. Biodegradable alloys, such as Mg, Fe, and Zn, are under investigation for their ability to degrade, being replaced by new bone. Ion-modified materials, in turn, aim to increase osteogenesis and antimicrobial action. Finally, mesenchymal stem cells can reduce inflammation and stimulate osteogenesis, enabling tissue differentiation. Furthermore, interaction with endothelial cells stimulates development, bone proliferation, and angiogenesis.

**Conclusion:** Autogenous grafts remain the gold standard for critical defects, but their limited supply hinders their use. Therefore, bioceramics, polymers, and metals are promising tools for bone regeneration. While synthetic polymers and traditional metals remain widely used, biodegradable materials and ion-modified biomaterials expand their therapeutic potential. The combination with mesenchymal stem cells represents an advanced and effective approach, with a positive impact on clinical reconstructive practice.

## Auricular Vagus Nerve Stimulation (AVNS) for Migraine

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**Introduction and Objectives:** Noninvasive stimulation of the auricular vagus nerve is a promising neuromodulation strategy for migraine management, considering that it is characterized by being a neurological condition with recurrent attacks of moderate to severe pain, usually accompanied by nausea, vomiting, and hypersensitivity to sensory stimuli. In this sense, it is worth noting that aVNS acts by transcutaneous stimulation of the auricular branch of the vagus nerve, reducing the frequency and intensity of seizures. Thus, it is expressed that the objective of the present study is to analyze the applicability in relation to safety and efficacy in the treatment of migraine.

**Methods:** A narrative review was conducted in order to evaluate the efficiency of auricular vagus nerve stimulation for the treatment of migraine. The study is based on systematic reviews/meta-analyses, randomized controlled trials, and functional neuroimaging studies. Platforms such as PubMed and EMBASE were used to search articles based on the following keywords: transcutaneous auricular vagus nerve stimulation, migraine disorders, neuromodulation, pain modulation, and chronic pain. Inclusion criteria included human studies in English, addressing migraine patterns, reporting pain and stimulation patterns, and clinical endpoints. Exclusion criteria included animal studies, invasive VNS, and conference abstracts without full data available.

**Results and Discussion:** Results demonstrate that only four weeks of aVNS at 1 Hz significantly modulated the default mode and vestibular cortical networks, increasing the connectivity of these areas (inferior temporal gyrus and parietal/orbitofrontal regions) and reducing the connectivity of other areas (cerebellum and motor areas), correlating with the decrease in headache. Meta-analyses demonstrate that low-frequency aVNS is capable of reducing the number of migraine days per month ( $MD \approx -1.8$  days/month) and pain intensity ( $SMD \approx -0.7$ ), with superior effects compared to higher frequencies. In the context of chronic pain, the results were more striking for pain reduction (Hedges'  $g \approx -1.95$ ), decreasing the intake of analgesic medication. Adverse effects were considered mild and transient.

**Conclusion:** It is concluded that aVNS represents a well-tolerated and effective alternative in the adjuvant treatment of migraine, with positive effects on pain reduction and frequency of attacks. The short-term low-frequency (1 Hz) application of aVNS modulated cortical pain networks, reducing the use of analgesics. Despite the promising results, more large, long-term studies are needed to confirm its clinical efficacy.

## Combination or Monotherapy? A Systematic Review Evaluating Treatment Strategies for Androgenetic Alopecia

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**Background and Objectives:** Androgenetic alopecia (AGA), known as male-pattern baldness or female-pattern hair loss, is the most common type of hair loss affecting men and women after the onset of puberty, predominantly affecting men. With the rising incidence of AGA, a variety of treatments have emerged, showing promising results when used in combination. This systematic review aims to compare the efficacy and safety of nonsurgical combination therapy versus monotherapy.

**Methods:** A comprehensive search of eight databases (last 10 years) identified studies comparing at least one combination therapy to a monotherapy for AGA in adults. The PICO was: P: Human adults diagnosed with AGA; I: Nonsurgical combination therapy (topical/oral minoxidil, topical finasteride, topical/oral spironolactone, oral bicalutamide 25 mg/d, topical 2% flutamide, oral vitamin D3, laser therapy (fractional, low-level), platelet-rich plasma, basic fibroblast growth factor, microneedling, secretome from adipose-derived stem cells and thread therapy using poly-L-lactic acid); C: Monotherapy using one of the above interventions or normal saline (placebo); O: Hair density, thickness, shaft diameter, hairs per follicular unit, physician global photographic assessment, patient-reported outcomes and adverse events. Risk of bias was independently assessed using the Cochrane RoB2 tools. Data were analyzed descriptively; no meta-analysis was performed because of heterogeneity. Ethical approval was not required.

**Results:** From 2,171 records, 44 studies (n = 3,254 patients; 2,032 males, 734 females and 261 with sex not reported) were selected. Designs included 20 studies with two arms, 18 with three arms, 4 split-scalp, and 2 with four arms. Varied combination therapy consistently produced greater improvements in objective hair parameters versus monotherapy. Dermatology Life Quality Index, and Women's AGA Quality of Life Questionnaire results were also higher in the combination groups. No significant adverse events were encountered, except: erythema, pruritus and injection-site pain. However, limitations included short follow-up ( $\leq 6$  months) and incomplete reporting of ethnicity.

**Conclusion:** Combination therapy appears more effective than monotherapy for AGA with minimal adverse effects. Randomized controlled trials with longer follow-up are necessary to confirm long-term safety and durability.