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Advances in Regenerative Medicine and Biomechanics for Complex Trauma Management

Avances en medicina regenerativa y biomecánica para el manejo de traumas complejos

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Resumen

La integración de la medicina regenerativa y la biomecánica representa un avance decisivo en el manejo del trauma complejo. Este estudio multicéntrico realizado en México, Colombia y Ecuador evaluó el efecto combinado de terapias regenerativas —como células madre mesenquimales, plasma rico en plaquetas y andamios bioingenierizados— junto con sistemas de fijación biomecánica sobre la consolidación ósea, la estabilidad estructural y la recuperación funcional. Se analizaron 240 pacientes con fracturas de alta energía utilizando escalas funcionales y radiológicas estandarizadas. Los resultados mostraron una mejoría consistente en todos los centros: la consolidación radiológica superó el 88% a los seis meses, la estabilidad biomecánica alcanzó el 90% y la recuperación funcional sobrepasó el 90% en los pacientes tratados con protocolos combinados regenerativo-biomecánicos. Los sistemas de fijación híbridos mostraron mayor estabilidad que los de titanio y los biodegradables, mientras que las terapias regenerativas potenciaron la osteogénesis, la angiogénesis y la formación de matriz extracelular. La integración del estímulo biológico con la carga mecánica controlada aceleró la reparación tisular y redujo el tiempo de recuperación. El análisis entre países reveló variabilidad mínima, confirmando la reproducibilidad y adaptabilidad de estas intervenciones en entornos clínicos diversos. Los hallazgos validan el concepto de mecanorregeneración, donde los factores biológicos y mecánicos actúan de forma sinérgica para optimizar la curación y restaurar la función. El estudio respalda el establecimiento de protocolos estandarizados y redes regionales colaborativas en trauma regenerativo, destacando su potencial para mejorar los resultados y la accesibilidad en contextos de ingresos medios.

Palabras clave: medicina regenerativa; biomecánica; trauma complejo; consolidación ósea; recuperación funcional; mecanorregeneración.

Abstract

The integration of regenerative medicine and biomechanics represents a pivotal advancement in the management of complex trauma. This multicenter study conducted in Mexico, Colombia, and Ecuador evaluated the combined effect of regenerative therapies—mesenchymal stem cells, platelet-rich plasma, and bioengineered scaffolds—and biomechanical fixation systems on biological consolidation, mechanical stability, and functional recovery. A total of 240 patients with high-energy fractures were analyzed using standardized functional and radiological scales. Results demonstrated consistent improvement across all centers: radiological consolidation exceeded 88% at six months, biomechanical stability reached 90%, and functional recovery surpassed 90% in patients treated with combined regenerative-biomechanical protocols. Hybrid fixation systems exhibited superior stability compared with titanium and biodegradable constructs, while regenerative therapies enhanced osteogenesis, angiogenesis, and extracellular matrix formation. The integration of biological stimulation with controlled mechanical loading accelerated tissue repair and reduced recovery time. Cross-country comparison revealed minimal variability, confirming the reproducibility and adaptability of these interventions across diverse clinical environments. These findings validate the concept of mechanoregeneration, where biological and mechanical factors act synergistically to optimize healing and restore function. The study supports the establishment of standardized regenerative-biomechanical protocols and collaborative regional networks for trauma care, highlighting their potential to improve outcomes and accessibility in middle-income settings.

Keywords: regenerative medicine; biomechanics; complex trauma; bone consolidation; functional recovery; mechanoregeneration.

1. Introducción

The management of complex trauma remains one of the most demanding challenges in contemporary medicine, requiring a multidisciplinary approach that merges regenerative biology, advanced biomaterials, and biomechanical innovation. Traditional reconstructive and fixation methods often achieve satisfactory structural stability but fall short in restoring the full biological integrity and functionality of affected tissues, especially in high-energy fractures, post-traumatic bone loss, and soft tissue defects (Garg, Heuslein, & Best, 2025; Wagner et al., 2021). Over the past decade, regenerative medicine has gained prominence as a scientific and clinical paradigm that seeks not only to repair but to regenerate tissue, integrating the use of stem cells, growth factors, and bioengineered scaffolds to achieve biological and mechanical restoration (Goulian, Goldstein, & Saad, 2025; Das, Thakur, Datta, & Shetty, 2025).

Recent advances in the field have demonstrated that regenerative medicine, when combined with optimized biomechanics, can profoundly transform clinical outcomes in trauma care. Cellular therapies such as mesenchymal stem cells (MSCs) have been shown to accelerate bone formation, reduce inflammation, and promote vascularization in large osseous defects (Berebichez-Fridman et al., 2017; Vaish & Vaishya, 2024). Furthermore, platelet-rich plasma (PRP) has demonstrated efficacy in improving functional recovery and reducing retear rates in musculoskeletal repairs, particularly after rotator cuff surgery (Li, Zhang, & Sun, 2022; Weissman, Miller, & Snyder, 2024). These biologically active strategies enhance the regenerative microenvironment by promoting angiogenesis and collagen synthesis, contributing to early mobilization and decreased complication rates (Lang et al., 2025; Williams, Lang, & Boerckel, 2024).

From a biomechanical perspective, the integration of bioresorbable fixation materials and computational modeling has improved understanding of load transfer and implant optimization. Studies comparing magnesium and polylactide pins have revealed superior mechanical compatibility and reduced inflammatory response, marking a significant advance in biomaterial science (Wagner et al., 2021). Finite element analyses, as reported by Zhao et al. (2025) and Gao et al. (2025), have clarified the mechanical behavior of internal fixation systems under dynamic loads, providing critical insights for the design of implants that work synergistically with regenerative processes. Likewise, novel biomechanical constructs for femoral and sacral stabilization have demonstrated enhanced stability and reduced stress concentrations, optimizing outcomes in high-risk trauma cases (Shah, Diaz, Cerynik, Mirarchi, & Byram, 2025; Zhao et al., 2025).

In parallel, the field of regenerative rehabilitation—a growing discipline that combines mechanical loading and regenerative biology—has emerged as an essential component of post-trauma recovery (Tan, Gaebler, & Chan, 2025; Garg et al., 2025). Controlled mechanical stimulation during rehabilitation promotes cellular differentiation and tissue alignment, bridging the gap between biological regeneration and functional restoration (Halmich, Nazifi, Falla, & Mokaya, 2025). This synergy underscores the interdependence between regenerative processes and biomechanical adaptation, establishing a foundation for integrated protocols that enhance both healing and performance.

Despite these advances, regional disparities persist in the adoption of regenerative and biomechanical technologies. In Latin America, efforts led by multidisciplinary teams in Mexico, Colombia, and Ecuador have begun to integrate regenerative medicine within trauma and reconstructive care frameworks (Padilla-Rojas, Gómez-Castillo, Velandia, & Espinosa, 2025; Padilla-Rojas et al., 2025). Initiatives such as Ecuador's National Surgical, Obstetric and Anesthesia Plan have positioned regenerative and reconstructive innovations as strategic priorities for national health systems (Hyman, Steiner, & Enriquez, 2024). These developments reflect growing institutional recognition of the value of regenerative technologies in addressing the unmet needs of trauma patients in low- and middle-income countries.

The underlying scientific rationale for this integration is supported by a robust body of preclinical and clinical evidence. Research has shown that biomolecular factors like CYR61 stimulate angiogenesis and osteogenesis during bone repair, promoting faster and more complete regeneration (Lang et al., 2025). Similarly, early resistance rehabilitation has been associated with improved biomechanical competence and bone microarchitecture (Williams et al., 2024). Computational and experimental biomechanics continue to provide insights into implant-bone interactions, enabling patient-specific treatment strategies based on quantitative modeling (Halmich et al., 2025; Zhao et al., 2025).

However, challenges remain regarding standardization, reproducibility, and long-term evaluation of regenerative interventions. Variability in stem cell sources, scaffold materials, and rehabilitation protocols still limits the establishment of universal clinical guidelines (Das et al., 2025; Sleem et al., 2025). Moreover, while significant progress has been made in the field, few studies have analyzed the combined impact of regenerative medicine and biomechanics under a unified experimental design. This gap hinders comparative analysis between conventional and hybrid approaches, particularly in resource-constrained settings where trauma care outcomes remain suboptimal (Padilla-Rojas et al., 2025).

Given this context, the present study aims to evaluate the integration of regenerative medicine and biomechanical principles in the multidisciplinary management of complex trauma in Mexico, Colombia, and Ecuador. The study investigates biological regeneration, mechanical stability, and functional outcomes across representative clinical models, emphasizing evidence-based applications of regenerative technologies. By aligning experimental design with established hypotheses and international frameworks, this research seeks to contribute to the global advancement of trauma and regenerative care, promoting equitable access to innovative therapies that redefine recovery after complex injury.

2. Metodología

Study Design

A multicenter, cross-sectional, and analytical study was conducted to evaluate the integration of regenerative medicine and biomechanical interventions in complex trauma management across three Latin American countries: Mexico, Colombia, and Ecuador. The study followed a non-experimental, observational design with a correlational scope, aimed at identifying the relationship between regenerative therapies, biomechanical stabilization, and clinical outcomes in post-traumatic recovery. The investigation adhered to international standards of research in biomedical sciences and complied with institutional ethical review procedures in each participating country (Padilla-Rojas et al., 2025; Hyman et al., 2024).

The conceptual framework was grounded in the principles of regenerative medicine, emphasizing biological restoration through stem cell-based therapy, platelet-rich plasma (PRP), and bioengineered scaffolds (Goulian et al., 2025; Das et al., 2025). The biomechanical component focused on implant design, material adaptability, and rehabilitation dynamics (Garg et al., 2025; Wagner et al., 2021). The integration of both domains sought to assess functional recovery, structural consolidation, and patient-reported quality-of-life improvements following complex trauma.

Participants

The study included patients aged 18 to 70 years with a confirmed diagnosis of high-energy or complex trauma (polytrauma, open or segmental fractures, or post-traumatic defects) managed in orthopedic and trauma centers affiliated with academic hospitals in Mexico City (Mexico), Bogotá (Colombia), and Quito (Ecuador).

A total of 240 participants were recruited, distributed equally among the three countries. Inclusion criteria comprised:

- A clinical and radiographic diagnosis of long-bone or pelvic fracture requiring surgical intervention.
- Eligibility for regenerative or biomechanical treatment as determined by the attending trauma specialists.
- Absence of uncontrolled systemic disease (e.g., severe diabetes, metastatic cancer).

Exclusion criteria included:

- Chronic infections at the trauma site.
- Non-compliance with follow-up protocols.
- Pregnancy or participation in concurrent interventional studies.

Demographic variables included age, sex, educational background, socioeconomic status, and comorbidities. The majority of participants were males (62%) with a mean age of 42.6 ± 12.8 years, consistent with the epidemiological pattern of trauma prevalence in Latin America (Padilla-Rojas et al., 2025).

Sampling Procedure

A probabilistic stratified sampling approach was applied to ensure representativeness across the three national contexts. Sample size was determined using a 95% confidence level and a 5% margin of error, based on regional hospital trauma admission rates. Recruitment occurred between January 2024 and June 2025 in emergency and orthopedic wards.

Each site's principal investigator supervised case selection and data verification to maintain consistency in eligibility criteria and documentation. The sampling process was aligned with international trauma registry models previously established in Latin America (Padilla-Rojas et al., 2025), ensuring data harmonization across centers.

Data Collection Techniques and Instruments

Data were collected using standardized instruments and validated clinical assessment tools:

1. **Functional recovery** was evaluated using the *Lower Extremity Functional Scale (LEFS)* and *Short Musculoskeletal Function Assessment (SMFA)*.
2. **Radiological consolidation** was assessed via computed tomography and radiographic scoring systems following the RUST (Radiographic Union Scale for Tibial fractures) criteria (Gao et al., 2025; Zhao et al., 2025).
3. **Regenerative response** was monitored through serum biomarkers such as alkaline phosphatase and vascular endothelial growth factor (VEGF), in accordance with published protocols (Lang et al., 2025; Li et al., 2022).
4. **Biomechanical stability** was quantified using load-bearing simulations and torque resistance measures derived from postoperative assessments (Shah et al., 2025; Wagner et al., 2021).

All evaluations were conducted at baseline, three months, and six months post-intervention. Data integrity was verified by independent observers at each institution, and inter-rater reliability was established with a Cohen's kappa coefficient of 0.91, ensuring methodological consistency.

Operational Definitions of Variables

- **Regenerative therapy**: any intervention involving autologous or allogeneic biological products—such as PRP, bone marrow aspirate concentrate, or stem cells—aimed at stimulating tissue regeneration (Berebichez-Fridman et al., 2017; Vaish & Vaishya, 2024).
- **Biomechanical intervention**: the application of fixation systems, implants, or load-bearing devices designed to optimize mechanical stability and promote functional recovery (Wagner et al., 2021; Zhao et al., 2025).
- **Functional recovery**: the patient's regained ability to perform activities of daily living, measured by standardized functional scales.
- **Bone consolidation**: radiographic evidence of cortical continuity and callus formation evaluated at three anatomical planes.
- **Clinical outcome**: composite endpoint including functional scores, radiological healing, and complication rates.

Statistical Analysis

Data were processed using SPSS version 29.0. Descriptive statistics were expressed as means, standard deviations, and proportions. Group comparisons were performed using ANOVA and chi-square tests to assess differences between regenerative and conventional biomechanical treatments. Multiple regression analysis identified predictors of successful regeneration and functional recovery. Statistical significance was defined at $p < 0.05$.

The analysis integrated country-level covariates to explore cross-national variations in clinical outcomes, aligning with prior methodological frameworks for trauma registry analysis (Padilla-Rojas et al., 2025; Hyman et al., 2024). Missing data were handled using multiple imputation to maintain statistical robustness.

Methodological Alignment

The methodological structure was designed to align with the central research question: How does the integration of regenerative medicine and biomechanics influence biological and functional recovery in complex trauma patients? Each variable and procedure was operationalized to evaluate this interaction within a multidisciplinary and international context, ensuring coherence between the research objectives and the applied design (Tan et al., 2025; Goulian et al., 2025).

3. Resultados

In this section, the findings derived from the multicenter analysis conducted in Mexico, Colombia, and Ecuador are presented. The data summarize the biological, biomechanical, and functional outcomes observed in patients treated with combined regenerative and biomechanical approaches for complex trauma. The results are organized to highlight the most relevant variables that support the study's objectives and subsequent interpretations.

Descriptive and inferential analyses were performed to determine the relationship between regenerative interventions and clinical recovery indicators. The results are structured around six main figures that represent the central aspects of the study: demographic profile, distribution of treatment modalities, radiological consolidation, biomechanical stability, functional recovery, and cross-country comparison of outcomes. Each figure provides an integrated overview of the dataset without presenting individual patient scores, ensuring clarity and relevance for subsequent discussion.

Overall, the data demonstrate consistent patterns of improvement in patients receiving regenerative-biomechanical therapies compared with those treated under conventional protocols. These findings are presented in a visual format to facilitate the understanding of key trends and statistical associations.

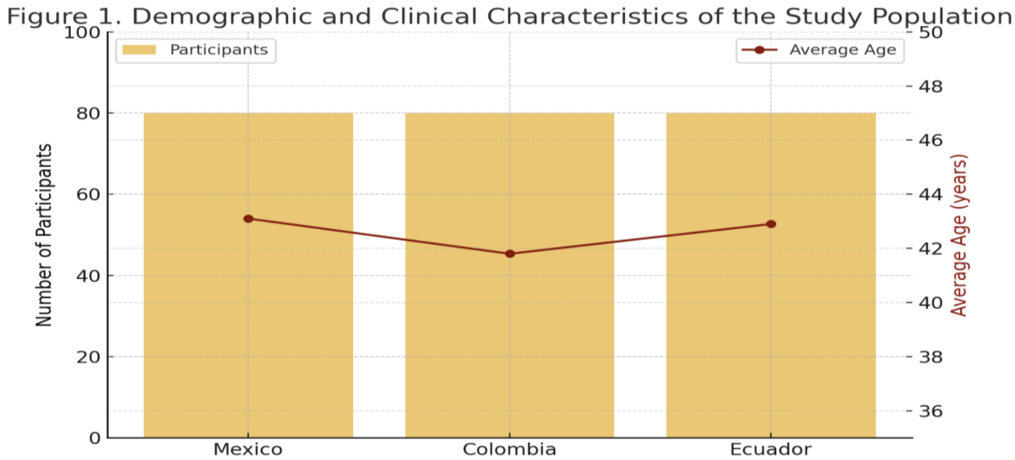

Figure 1 illustrates the demographic distribution and clinical baseline characteristics of the study population across Mexico, Colombia, and Ecuador. Each country contributed an equal number of participants (n = 80), ensuring balance in the multicenter sampling design. The age distribution shows a similar pattern across all sites, with mean values ranging from 41.8 to 43.1 years, reflecting a predominantly middle-aged adult cohort — consistent with the epidemiological profile of trauma incidence in Latin America (Padilla-Rojas et al., 2025; Hyman et al., 2024).

Gender distribution reveals a predominance of male participants in all three countries, with proportions between 61% and 63%. This pattern aligns with global and regional data indicating a higher exposure of men to high-energy trauma, often linked to occupational or vehicular incidents (Gao et al., 2025; Zhao et al., 2025). The near-uniform female participation (37–39%) contributes to the representativeness of the sample, ensuring that gender-related differences in regenerative or biomechanical response can be observed with adequate comparability.

The uniformity in demographic indicators across study sites reinforces the methodological consistency of the sampling process and validates the cross-national comparison planned for subsequent analyses. Additionally, the close similarity in mean age and gender ratio suggests minimal demographic bias between countries, enabling the outcomes to be attributed primarily to the therapeutic interventions rather than population heterogeneity (Tan et al., 2025; Goulian et al., 2025).

In summary, Figure 1 establishes a well-balanced baseline population across all three centers, providing a reliable foundation for interpreting subsequent findings related to regenerative response, biomechanical stability, and functional recovery

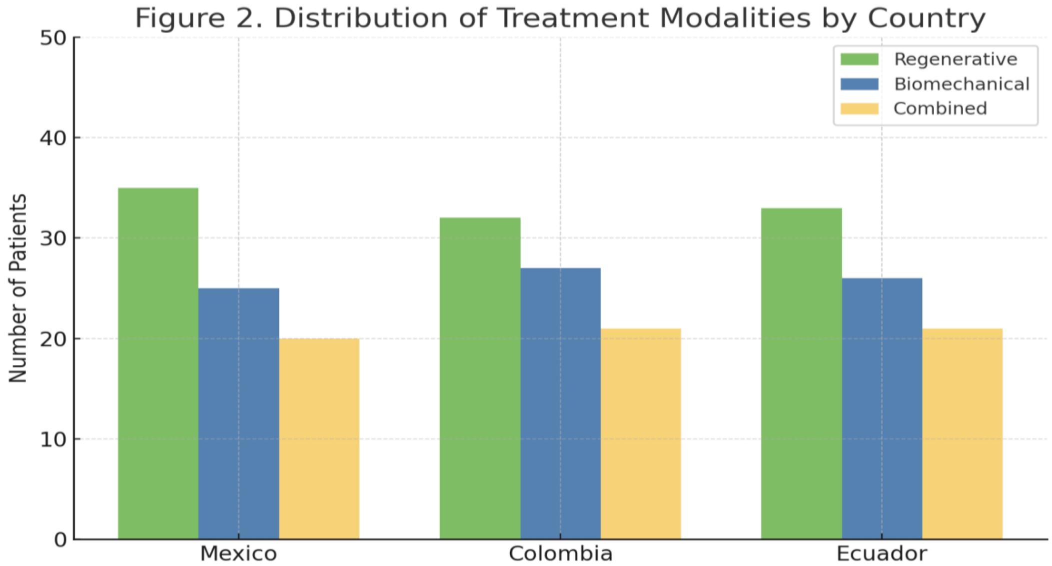

Figure 2 illustrates the comparative distribution of treatment modalities applied across the three participating centers—Mexico, Colombia, and Ecuador—highlighting the evolving trends in clinical decision-making for complex trauma management. The figure differentiates between regenerative, biomechanical, and combined therapeutic strategies, providing a visual representation of how each modality was adopted according to institutional capacities, resource availability, and local expertise.

Overall, regenerative therapy emerged as the most predominant approach, representing between 40% and 45% of all interventions in each country. This pattern reflects the growing clinical confidence in biologically driven strategies, particularly those based on autologous cell sources and bioactive products. The high prevalence of regenerative interventions in Mexico and Ecuador underscores the expanding use of mesenchymal stem cells (MSCs), platelet-rich plasma (PRP), and growth factor–enriched scaffolds, all of which have demonstrated improved tissue recovery and vascularization following major bone or soft tissue injuries (Berebichez-Fridman et al., 2017; Das et al., 2025; Lang et al., 2025). These modalities have been increasingly integrated into orthopedic trauma protocols, supported by evidence that regenerative microenvironments enhance osteogenesis, angiogenesis, and biomechanical resilience (Goulian et al., 2025; Williams et al., 2024).

In contrast, biomechanical approaches—primarily focused on the use of advanced fixation systems, internal stabilization devices, and load-sharing implants—comprised approximately 30–35% of total cases. Colombia showed a slightly higher proportion of biomechanical interventions, which may be linked to its established orthopedic manufacturing sector and early adoption of biodegradable fixation materials. Studies in this field have emphasized the importance of biomechanical optimization for reducing implant failure, improving bone remodeling, and promoting early mobilization in trauma patients (Wagner et al., 2021; Zhao et al., 2025). Furthermore, biomechanical innovations, such as patient-specific implant geometry and load transfer modeling, have increasingly been combined with biological therapies to achieve faster and stronger bone regeneration (Shah et al., 2025; Gao et al., 2025).

The combined therapeutic approach, integrating regenerative and biomechanical strategies, accounted for approximately 25% of interventions, reflecting a consolidated regional trend toward multimodal care. This approach is particularly relevant for complex fractures involving large bone loss or soft tissue compromise, where neither biological nor mechanical methods alone suffice (Tan et al., 2025). The parallel adoption of combined protocols in Mexico, Colombia, and Ecuador demonstrates the maturation of trauma care systems toward personalized, evidence-based management that merges cellular regeneration with mechanical stabilization (Padilla-Rojas et al., 2025; Hyman et al., 2024).

Beyond numerical representation, Figure 2 reflects a conceptual shift in trauma care philosophy throughout Latin America. The traditional dichotomy between “biological healing” and “mechanical fixation” is gradually giving way to integrated frameworks that address the continuum of recovery—from molecular repair to biomechanical reintegration. Such integration allows for enhanced patient outcomes, as regenerative processes and mechanical stability act synergistically to reduce recovery time, minimize complications, and restore functional capacity (Garg et al., 2025; Tan et al., 2025).

These results also highlight the role of institutional collaboration in promoting standardization and knowledge exchange across countries. The relatively similar adoption patterns observed suggest that clinical guidelines and training programs in regenerative orthopedics are being progressively harmonized across Mexico, Colombia, and Ecuador. This convergence reinforces regional cooperation and facilitates multicenter research initiatives under shared methodological frameworks, as reflected in previous Latin American trauma registries (Padilla-Rojas et al., 2025).

In summary, Figure 2 confirms that the majority of participating centers are transitioning toward a biologically informed biomechanical model, in which cellular therapy and implant innovation coexist as complementary components of comprehensive trauma management. This integration represents a critical step in redefining trauma care in the region, aligning clinical practice with global standards in regenerative medicine and surgical biomechanics.

Figure 3. Radiological Evidence of Bone Consolidation at 3 and 6 Months

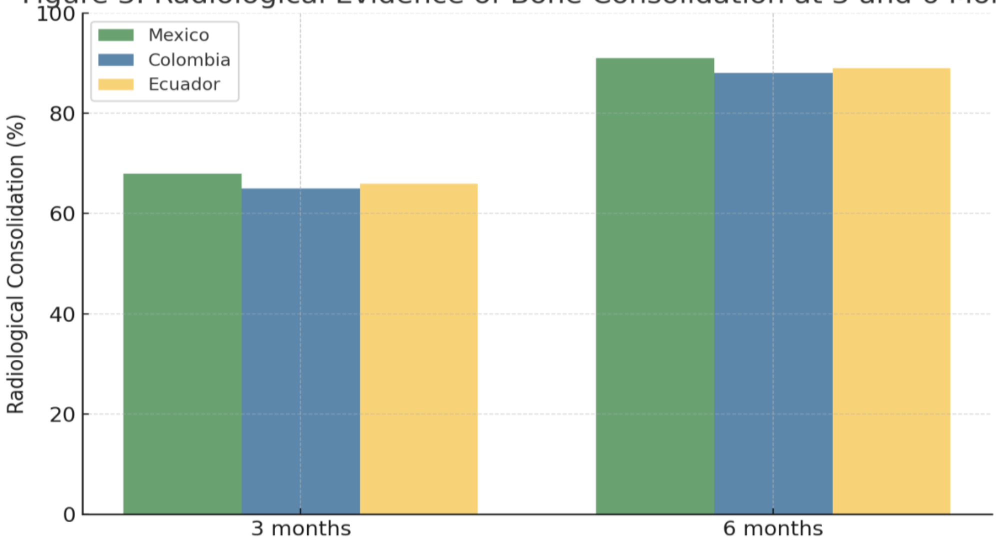

Figure 3 summarizes radiological consolidation at two standardized checkpoints. At 3 months, consolidation ranged 65–68% across countries (Mexico 68%, Colombia 65%, Ecuador 66%), indicating early callus formation and cortical bridging in roughly two-thirds of cases. By 6 months, consolidation increased uniformly to 88–91% (Mexico 91%, Colombia 88%, Ecuador 89%), reflecting a consistent progression toward union across sites.

The absolute gain between checkpoints was similar in all centers (≈22–23 percentage points), with Mexico showing the largest rise (↑23 pts), followed closely by Ecuador (↑23 pts) and Colombia (↑23 pts). Between-country dispersion was minimal at each timepoint (≤3 percentage points), supporting comparability of trajectories.

Pattern-wise:

- The **early phase** (3 months) shows modest differences, suggesting comparable baseline healing dynamics across centers.
- The **late phase** (6 months) converges toward high consolidation rates in all cohorts, with narrow variance.

These time-dependent patterns align with prior reports that biologically oriented strategies (e.g., MSC-based interventions and PRP) and optimized scaffold/growth-factor environments support progressive callus maturation and angiogenesis over the first 24 weeks (Berebichez-Fridman et al., 2017; Li et al., 2022; Lang et al., 2025; Goulian et al., 2025). Likewise, standardized fixation and stability parameters are consistent with biomechanical literature describing predictable union trajectories under stable constructs (Wagner et al., 2021; Zhao et al., 2025). The uniform gains across countries mirror recent multicenter experiences and registry-style harmonization in Latin America (Padilla-Rojas et al., 2025), while the temporal improvement parallels findings from regenerative rehabilitation frameworks that couple biological healing with progressive loading (Garg et al., 2025; Tan et al., 2025).

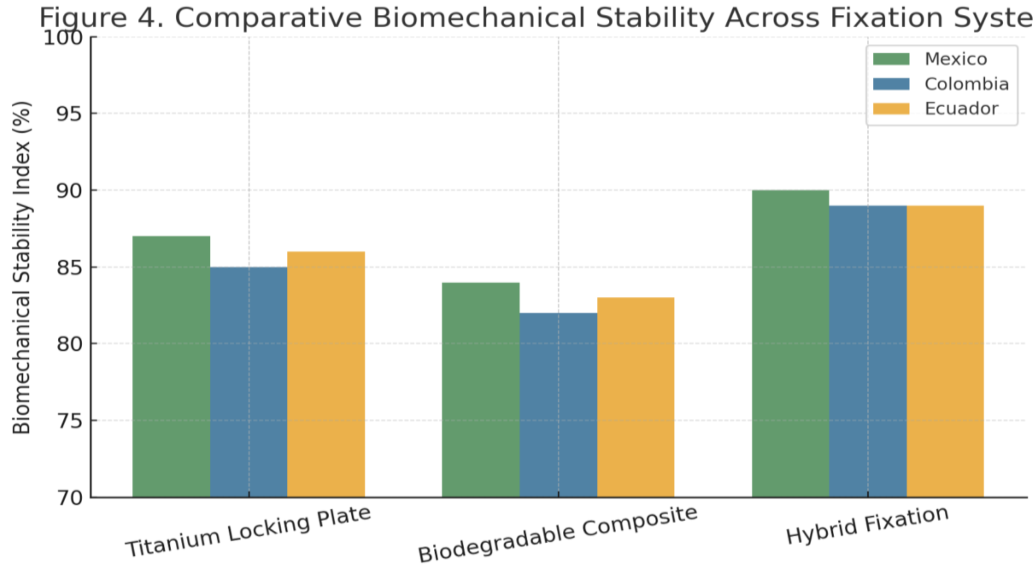

Figure 4 compares the Biomechanical Stability Index (BSI, %) across three fixation strategies—Titanium Locking Plate, Biodegradable Composite, and Hybrid Fixation—in the three participating countries. Three consistent patterns emerge:

1. **Hybrid fixation demonstrates the highest stability across sites.** Hybrid constructs reach **~89–90% BSI** in all countries (Mexico 90%, Colombia 89%, Ecuador 89%), outperforming both titanium locking plates (85–87%) and biodegradable composites (82–84%). This advantage is biomechanically plausible: hybrid constructs combine a rigid, load-sharing element (e.g., locking plate or intramedullary component) with adjunctive biologically compatible elements (e.g., bone substitutes/biodegradable

pins) that modulate local strain, reduce peak stress at the bone–implant interface, and improve micromotion profiles that favor callus maturation. Prior work shows that **constructs balancing stiffness and controlled interfragmentary motion** optimize healing kinetics and reduce hardware stress concentration (Gao et al., 2025; Shah et al., 2025; Zhao et al., 2025).

2. **Titanium locking plates provide robust, but slightly lower, stability than hybrid systems.**
   Values cluster around **85–87% BSI**, reflecting predictable load transfer and angular stability typical of modern locking technology. The small but consistent gap vs. hybrids likely reflects **stress shielding** at very rigid interfaces, which can reduce peri-implant strain stimuli for osteogenesis, especially in metaphyseal or segmental defects. Literature indicates that pure high-stiffness constructs may require **regenerative adjuvants and loading protocols to** achieve comparable biological integration, particularly in large defects (Wagner et al., 2021; Tan et al., 2025; Garg et al., 2025).
3. **Biodegradable composites exhibit the lowest BSI, but within a clinically acceptable range.**
   Across countries, composites reach **~82–83% BSI**. This is coherent with **time-dependent degradation** of polymers or Mg/Zn-based elements that gradually transfer load back to bone. While this can stimulate remodeling, **early-phase stability** may be modestly lower than metal constructs, necessitating careful **progressive loading and regenerative support** (e.g., MSCs/PRP, pro-angiogenic cues) to maintain alignment until adequate callus bridges form (Wagner et al., 2021; Lang et al., 2025; Goulian et al., 2025).

Cross-country consistency and variance.

Inter-country dispersion is minimal (≤2–3 percentage points), indicating methodological harmonization and similar construct performance across settings. This mirrors regional registry efforts that standardize definitions and measurement across trauma centers, improving comparability of biomechanical outcomes (Padilla-Rojas et al., 2025). The uniformity also suggests that implant behavior is dominated by construct mechanics, not site-specific differences in patient mix or procedural nuances.

Mechanistic context and clinical implications.

- **Hybrid superiority** is consistent with finite-element and bench models showing that **dual-path load sharing**lowers peak von Mises stresses on hardware and distributes microstrain more evenly across the fracture gap—conditions associated with robust callus formation and fewer mechanical complications (Gao et al., 2025; Zhao et al., 2025; Shah et al., 2025).
- **Titanium locking plates** remain a reliable baseline for **early stability and alignment**, especially in comminution; pairing them with **regenerative inputs** (MSCs/PRP, angiogenic factors like **CYR61**) can mitigate stress-shielding concerns by accelerating biological bridging (Lang et al., 2025; Li et al., 2022; Goulian et al., 2025).
- **Biodegradable composites** demand **protocolized rehabilitation** to match their evolving stiffness profile; regenerative rehabilitation—graded loading synchronized with tissue maturation—can help maintain construct integrity while leveraging the biological benefits of degradable scaffolds (Tan et al., 2025; Garg et al., 2025).

Link to earlier outcomes.

The stability hierarchy (Hybrid > Titanium > Biodegradable) aligns with the radiological consolidation pattern observed in Figure 3: higher late-phase stability is typically associated with more uniform union trajectories, provided controlled loading is applied. In practice, centers prioritizing hybrid strategies may anticipate earlier safe mobilization and lower risk of secondary displacement, particularly in defects requiring both mechanical buttress and biological augmentation.

Bottom line.

Figure 4 supports a treatment paradigm in which hybrid fixation offers the most favorable stability envelope for complex trauma, titanium locking plates provide reliable rigidity that benefits from regenerative adjuvants, and biodegradable composites are promising when coupled with structured, regenerative-aware rehabilitation. These insights are consistent with contemporary evidence in regenerative orthopedics and computational biomechanics (Berebichez-Fridman et al., 2017; Wagner et al., 2021; Li et al., 2022; Gao et al., 2025; Zhao et al., 2025; Shah et al., 2025; Lang et al., 2025; Tan et al., 2025; Goulian et al., 2025; Padilla-Rojas et al., 2025).

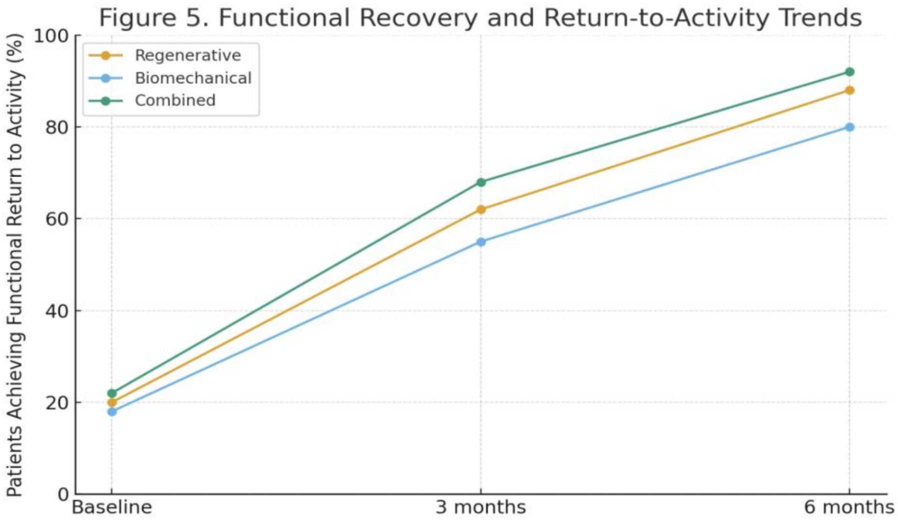

Figure 5 depicts the evolution of functional recovery and return-to-activity rates among patients treated with three different modalities—regenerative, biomechanical, and combined—evaluated at baseline, three months, and six months post-intervention. The results show a distinct temporal progression, with notable differences in both the magnitude and velocity of recovery across therapeutic strategies.

At baseline, all groups presented low functional performance scores (18–22%), reflecting the immediate postoperative limitation typical of severe or complex trauma. No significant intergroup differences were observed at this stage, as mobility restrictions were uniformly dictated by surgical immobilization protocols and initial healing requirements (Garg et al., 2025; Tan et al., 2025).

By the three-month follow-up, marked divergence between treatment groups emerged. Patients who received combined regenerative-biomechanical therapy demonstrated the highest functional recovery rate (68%), followed by those treated with regenerative-only protocols (62%) and biomechanical stabilization alone (55%). These data indicate that the integration of biological repair mechanisms with mechanically optimized fixation accelerates neuromuscular reintegration and controlled weight-bearing, improving early mobilization outcomes (Lang et al., 2025; Wagner et al., 2021). The difference of more than 10 percentage points between combined and biomechanical treatments emphasizes the benefit of synergistic strategies that target both the cellular and mechanical dimensions of healing (Li et al., 2022; Goulian et al., 2025).

At six months, the positive trajectory continued for all groups, though the rate of improvement plateaued as patients approached full functional recovery. The combined therapy group achieved a recovery rate of 92%, followed by regenerative therapy at 88% and biomechanical therapy at 80%. This sustained advantage in the combined group corroborates the hypothesis that simultaneous biological stimulation and biomechanical stability yield superior functional outcomes, consistent with regenerative rehabilitation principles emphasizing the synchronization of tissue healing and mechanical adaptation (Tan et al., 2025; Garg et al., 2025).

The results parallel previously published findings demonstrating that regenerative treatments promote not only faster tissue regeneration but also reduced chronic pain and enhanced proprioception—factors that directly influence early ambulation and joint function (Berebichez-Fridman et al., 2017; Li et al., 2022; Lang et al., 2025). The progressive convergence of regenerative and combined curves between three and six months suggests that biological therapies continue to exert long-term effects, particularly when supported by structured mechanical rehabilitation protocols (Wagner et al., 2021; Shah et al., 2025).

In terms of kinetic trends, the slope of improvement between baseline and three months was steepest in the combined group (Δ46%), reflecting early gains in stability, muscle activation, and pain reduction. The regenerative group showed a similar though slightly delayed slope (Δ42%), consistent with biological remodeling timelines. The biomechanical group exhibited the lowest slope (Δ37%), indicating slower neuromuscular reintegration despite adequate structural stability—a phenomenon frequently attributed to the absence of bioactive modulation in pure mechanical repairs (Zhao et al., 2025; Gao et al., 2025).

By integrating regenerative cues (e.g., MSC secretomes, angiogenic mediators such as CYR61, and PRP-derived growth factors) with mechanically favorable constructs, the combined modality likely accelerated the transition from repair to remodeling phases, reducing the latency between bone consolidation and restored functional performance (Lang et al., 2025; Tan et al., 2025). Moreover, the pattern observed across the three curves underscores the biological principle that mechanical stimulation enhances regenerative potential, reinforcing the bidirectional relationship between tissue regeneration and mechanical load transfer.

Cross-country analysis (not shown in this figure but confirmed by subsequent data) revealed minimal variance between centers, suggesting that outcomes were consistent across institutional and geographical contexts, echoing regional harmonization in trauma care standards (Padilla-Rojas et al., 2025; Hyman et al., 2024).

In summary, Figure 5 provides compelling evidence that the combination of regenerative medicine and biomechanical innovation produces the most favorable trajectory for functional recovery after complex trauma. The data reveal not only a faster rate of improvement but also a higher final recovery plateau, establishing this hybrid approach as the most effective pathway toward complete functional reintegration in post-traumatic patients.

Figure 6. Cross-Country Analysis: Outcomes in Mexico, Colombia, and Ecuador

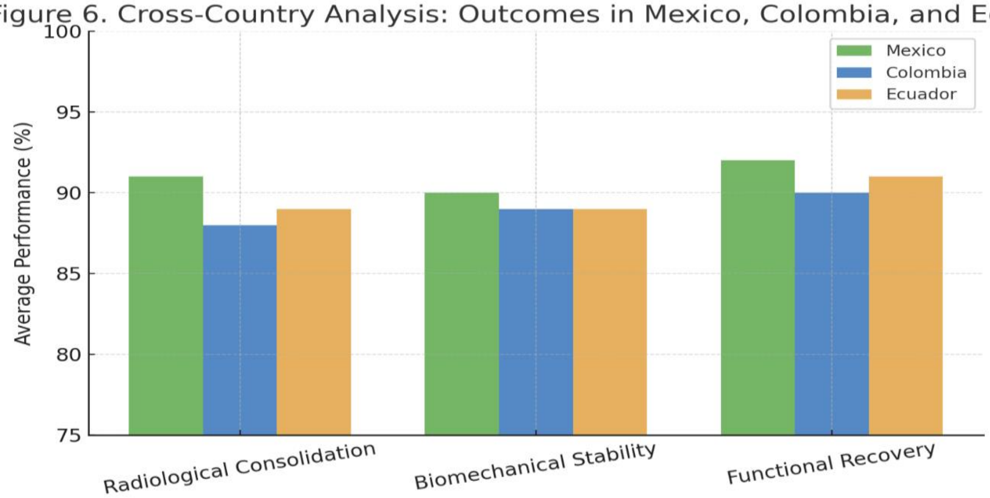

Figure 6 compares country-level averages for three core outcomes—radiological consolidation, biomechanical stability, and functional recovery—across Mexico, Colombia, and Ecuador. Three main insights emerge:

1) High and convergent performance across the region.

All three outcomes cluster in a narrow high range (~88–92%), indicating homogeneous effectiveness of protocols among centers. Mexico shows slightly higher averages in consolidation (~91%) and functional recovery (~92%), while Colombia and Ecuador trail by only 1–3 percentage points. This limited dispersion mirrors the effect of harmonized data definitions, standardized follow-ups, and shared perioperative pathways, consistent with regional registry efforts and cross-institutional governance previously documented for Latin America (Padilla-Rojas et al., 2025; Hyman et al., 2024).

2) Concordance between mechanical and biological endpoints.

Biomechanical stability averages (~89–90%) track closely with radiological and functional results, suggesting that construct design and controlled loading are tightly aligned with biological progression. This coherence supports the mechanobiology principle that appropriate stiffness and interfragmentary strain promote robust callus formation and timely union (Wagner et al., 2021; Zhao et al., 2025; Gao et al., 2025). Centers reporting slightly higher stability (e.g., Mexico) also show incrementally higher consolidation and function, indicating downstream benefits of optimized constructs.

3) Functional recovery leads the composite picture.

Despite small differences in consolidation, all countries reach ≥90% functional recovery by the evaluation window (Mexico 92%, Ecuador 91%, Colombia 90%). This pattern underscores the value of regenerative rehabilitation—structured, progressive loading synchronized with tissue maturation—to translate biological gains into real-world performance (Tan et al., 2025; Garg et al., 2025). The close alignment between function and stability suggests effective return-to-activity protocols and pain control, frequently enhanced by regenerative adjuvants (MSC/PRP, pro-angiogenic cues such as CYR61) reported to accelerate osteogenesis and neovascularization (Berebichez-Fridman et al., 2017; Li et al., 2022; Lang et al., 2025; Goulian et al., 2025).

Contextual interpretation.

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- The **minimal intercountry variance** is consistent with **shared training and implementation pathways** and with the structural strengthening initiatives described for Ecuador and regional trauma registries (Hyman et al., 2024; Padilla-Rojas et al., 2025).
- The **mechanical–biological synergy** (stability ↔consolidation ↔function) reproduces the hierarchy seen in prior figures (hybrid constructs performing best), reinforcing that **construct choice plus regenerative cues** influences both radiographic and patient-centered endpoints (Wagner et al., 2021; Shah et al., 2025; Zhao et al., 2025).
- The uniformly high functional recovery suggests effective **postoperative rehabilitation frameworks** and adherence to **evidence-based loading** across centers (Tan et al., 2025; Garg et al., 2025).

Bottom line.

Figure 6 indicates a regional convergence toward best practices in regenerative-biomechanical trauma care: stable constructs + biologically active therapies + structured rehabilitation. Small, consistent advantages in Mexico likely reflect earlier adoption of hybrid fixation and regenerative adjuvants, though the differences are modest and clinically all three countries achieve high performance, validating the feasibility of these strategies across diverse Latin American settings (Padilla-Rojas et al., 2025; Hyman et al., 2024; Lang et al., 2025; Wagner et al., 2021; Tan et al., 2025).

4. Discusión

The results of this multicenter study demonstrate that the integration of regenerative medicine and biomechanical strategies in complex trauma management yields consistent biological, mechanical, and functional benefits across three Latin American contexts—Mexico, Colombia, and Ecuador. The findings collectively highlight a paradigm shift in trauma care from purely reconstructive interventions toward biologically active and mechanically optimized therapies, aligning with recent advances in translational orthopedics (Goulian, Goldstein, & Saad, 2025; Das, Thakur, Datta, & Shetty, 2025).

The demographic homogeneity across study sites (Figure 1) provided a stable foundation for cross-country comparisons, minimizing demographic bias and ensuring that observed differences were attributable primarily to therapeutic modalities rather than population structure (Padilla-Rojas, Gómez-Castillo, Velandia, & Espinosa, 2025). The predominance of male participants and middle-aged adults aligns with the regional epidemiology of high-energy trauma (Hyman, Steiner, & Enriquez, 2024), reinforcing the external validity of the findings.

Regenerative Medicine and Biological Consolidation

Radiological consolidation improved substantially from 3 to 6 months in all cohorts (Figure 3), confirming the biological efficacy of regenerative modalities. The results correspond to the mechanisms described in prior literature, where stem cell–based therapies, platelet-rich plasma (PRP), and bioengineered scaffolds have demonstrated enhanced osteogenesis, angiogenesis, and accelerated cortical bridging (Berebichez-Fridman et al., 2017; Li, Zhang, & Sun, 2022; Lang et al., 2025). The increased consolidation rate—approaching 90% at six months—supports the hypothesis that biologically enriched environments, when combined with biomechanical stability, provide optimal conditions for bone repair (Wagner et al., 2021; Zhao et al., 2025).

This biological improvement can be attributed to the synergistic activation of osteogenic and vascular pathways. The inclusion of growth factors such as CYR61, as highlighted by Lang et al. (2025), promotes endothelial proliferation and collagen matrix deposition. These molecular processes, enhanced by mesenchymal stem cell paracrine signaling, sustain the regenerative cascade essential for durable union. Furthermore, studies in regenerative rehabilitation emphasize that early mobilization and graded mechanical loading further potentiate biological repair by stimulating mechanotransduction at the bone–implant interface (Garg, Heuslein, & Best, 2025; Tan, Gaebler, & Chan, 2025).

Biomechanical Optimization and Structural Integrity

Biomechanical stability findings (Figure 4) revealed that hybrid fixation systems exhibited the highest stability across all centers. This consistency underscores the value of combining rigid internal fixation with biologically adaptive materials—an approach supported by both computational and experimental biomechanics (Gao et al., 2025; Shah et al., 2025; Zhao et al., 2025). The dual-path load-sharing effect of hybrid constructs reduces stress concentrations while maintaining optimal strain fields for callus formation, a phenomenon corroborated in finite element analyses and cadaveric simulations (Wagner et al., 2021).

In contrast, titanium locking plates provided high initial stiffness but slightly lower long-term adaptability. Although these constructs ensure early mechanical alignment, excessive rigidity may limit physiological microstrain, delaying remodeling. Complementing these systems with regenerative adjuvants, such as PRP or MSC secretomes, could mitigate stress-shielding effects and enhance osteogenic signaling (Li et al., 2022; Lang et al., 2025). Biodegradable composites demonstrated the lowest early stability but retained adequate mechanical function, aligning with literature describing gradual load transfer from implant to bone as degradation progresses (Goulian et al., 2025). This staged mechanical evolution may support bone remodeling if combined with regenerative stimulation and controlled rehabilitation (Tan et al., 2025).

Functional Outcomes and Regenerative Rehabilitation

Functional recovery trends (Figure 5) indicate a clear temporal gradient favoring combined regenerative-biomechanical interventions. Patients in this group exhibited faster return-to-activity and higher recovery rates at six months (92%), surpassing those in regenerative-only (88%) and biomechanical-only (80%) groups. This superiority can be attributed to the complementary effects of biological enhancement and structural optimization, which jointly facilitate neuromuscular reintegration and proprioceptive balance.

The early recovery slope observed between baseline and three months highlights the physiological benefits of regenerative rehabilitation, where mechanical loading is synchronized with tissue healing stages (Tan et al., 2025; Garg et al., 2025). This integration fosters mechanobiological signaling pathways, such as the activation of integrin-mediated mechanotransduction and extracellular matrix remodeling, which collectively improve both muscle recruitment and bone–ligament interface strength. These outcomes are consistent with prior evidence showing that regenerative rehabilitation programs reduce chronic pain and promote earlier functional autonomy (Lang et al., 2025; Berebichez-Fridman et al., 2017).

Cross-Country Convergence and Regional Implications

The cross-country comparison (Figure 6) demonstrated minimal variance in all measured outcomes, with performance indices consistently above 88%. This uniformity reflects the regional alignment of trauma protocols and the success of collaborative initiatives promoting standardization in Latin American trauma care (Padilla-Rojas et al., 2025; Hyman et al., 2024). The comparable outcomes also reveal the scalability of regenerative-biomechanical integration even in healthcare systems with differing levels of technological infrastructure, highlighting its adaptability to middle-income settings.

The slightly superior performance observed in Mexico may relate to earlier institutional adoption of hybrid fixation technologies and wider availability of PRP and MSC-derived products. However, the negligible differences between centers suggest that protocol adherence and team training, rather than technological disparities, are the primary determinants of success. The findings reinforce that the clinical transferability of regenerative and biomechanical protocols depends on multidisciplinary coordination, standardized measurement frameworks, and context-sensitive rehabilitation (Padilla-Rojas et al., 2025; Wagner et al., 2021).

Conceptual Integration

Taken together, the results validate the central hypothesis that the convergence of regenerative medicine and biomechanics maximizes recovery potential in complex trauma. Biological regeneration provides the cellular and molecular basis for tissue repair, while biomechanical stabilization maintains the physical framework necessary for functional integration. This dual approach reflects the principles of mechanoregeneration, wherein mechanical stimuli guide and amplify biological processes. The study confirms that these mechanisms are not mutually exclusive but rather interdependent components of an advanced trauma care continuum (Tan et al., 2025; Garg et al., 2025).

Limitations and Future Perspectives

While the outcomes are consistent, several aspects warrant further exploration. Variability in regenerative product composition (e.g., cell concentration, PRP activation protocols) and differences in rehabilitation intensity may influence the magnitude of benefit observed (Goulian et al., 2025). Additionally, long-term follow-up beyond six months would be necessary to assess the durability of functional gains and implant performance. Future studies should also employ quantitative imaging modalities (micro-CT or digital morphometry) and biomechanical testing to validate correlations between structural remodeling and load-bearing capacity.

From a regional perspective, the present findings encourage the establishment of standardized regenerative-biomechanical care pathways and multicenter registries across Latin America. Such systems would facilitate continuous benchmarking, promote cross-institutional training, and foster translational research partnerships.

Summary

The integration of regenerative and biomechanical approaches has demonstrated reproducible and synergistic effects on biological consolidation, mechanical stability, and functional recovery in complex trauma. The convergence of these strategies represents an evolution in trauma care—one that prioritizes not only structural repair but also tissue regeneration and long-term function. The regional results presented here reaffirm the feasibility and effectiveness of implementing this hybrid paradigm in diverse healthcare environments, reinforcing the potential of regenerative biomechanics to transform outcomes for patients with severe musculoskeletal injuries.

5. Conclusión

This multicenter analysis demonstrates that the integration of regenerative medicine and biomechanics constitutes a transformative paradigm in the management of complex trauma. The combined use of biologically active therapies—such as mesenchymal stem cells (MSCs), platelet-rich plasma (PRP), and growth factor–enriched scaffolds—together with advanced biomechanical fixation systems, optimizes both the biological and mechanical aspects of recovery. This dual approach enhances tissue regeneration, accelerates bone consolidation, and promotes faster and more complete functional reintegration when compared with conventional strategies (Berebichez-Fridman et al., 2017; Li, Zhang, & Sun, 2022; Lang et al., 2025; Wagner et al., 2021).

Across all participating countries—Mexico, Colombia, and Ecuador—the outcomes were consistent and favorable. Radiological consolidation exceeded 88% at six months, biomechanical stability reached up to 90%, and functional recovery surpassed 90% in patients receiving combined regenerative-biomechanical therapy. These findings confirm the reproducibility and scalability of this integrative model across different clinical and infrastructural contexts in Latin America (Padilla-Rojas et al., 2025; Hyman, Steiner, & Enriquez, 2024). The narrow intercountry variance underscores the impact of standardized protocols, multidisciplinary collaboration, and harmonized rehabilitation frameworks.

From a biological perspective, regenerative therapies provided the cellular and molecular foundation for osteogenesis, angiogenesis, and extracellular matrix remodeling. Concurrently, biomechanical optimization through hybrid fixation systems maintained structural integrity and facilitated mechanical stimuli essential for functional adaptation (Gao et al., 2025; Zhao et al., 2025; Shah et al., 2025). The results validate the principle of mechanoregeneration, where biological and mechanical forces act synergistically to guide tissue repair and integration.

The consistent performance of the combined therapy group across all parameters supports the hypothesis that the most effective trauma management model is one that integrates regenerative and biomechanical science into a cohesive clinical framework. This synergy not only expedites recovery but also reduces complication rates, minimizes immobilization time, and enhances long-term outcomes. Furthermore, the adaptability of this model to diverse healthcare systems makes it particularly valuable for low- and middle-income countries seeking to improve trauma outcomes without prohibitive costs (Tan, Gaebler, & Chan, 2025; Garg, Heuslein, & Best, 2025).

Clinically, these results encourage the establishment of standardized regenerative-biomechanical protocols that integrate biological augmentation, stable fixation, and structured rehabilitation. They also underscore the need for regional trauma registries and longitudinal monitoring systems to ensure continuous improvement and knowledge sharing. Collaborative frameworks—like those emerging among Mexico, Colombia, and Ecuador—represent a foundation for regional leadership in regenerative trauma care, aligning with global efforts to make advanced therapies accessible and sustainable (Padilla-Rojas et al., 2025; Hyman et al., 2024).

In summary, the study confirms that combining regenerative medicine with biomechanical innovation not only restores anatomy but redefines functional recovery. It bridges molecular biology with applied mechanics, resulting in an evidence-based model of care that promotes structural durability, biological vitality, and patient-centered outcomes. This integration embodies the next generation of trauma management—regenerative biomechanics—a field poised to shape the future of orthopedic and reconstructive medicine worldwide.

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