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Review

A comparation of Cellular Technologies used in Vertebrology

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Abstract

Spinal fusion is one of the most common methods of treating spinal injuries, but despite improvements in implant designs, the incidence of pseudoarthrosis remains high. In this regard, there is growing interest in cell technologies aimed at enhancing osteogenesis.
A literature search was conducted in the PubMed, Web of Science, and Google Scholar databases for the period 2016 - 2025. The analysis included clinical studies, systematic reviews, and meta-analyses on the use of cell technologies in spondylodesis of the thoracic and lumbar spine. The review examines the use of mesenchymal stromal cells, bone marrow aspirate, stromal - vascular fraction, bone morphogenetic proteins, bioactive peptides, and autologous growth factors. Analysis of the literature shows that the use of cell technologies contributes to the enhancement of regenerative processes in spinal fusion and improves clinical treatment outcomes. Cell technologies represent a promising direction for improving the effectiveness of spinal fusion. Further research should focus on standardising application protocols and studying long-term treatment outcomes.

Keywords: thoracic and lumbar spine, spinal fusion, mesenchymal stromal cells, bone morphogenetic protein, stromal vascular fraction, bone marrow aspirate, cell-based therapies.

1. Introduction

Spinal fusion is currently one of the most commonly performed surgical procedures for the treatment of various spinal pathologies [1]. It is widely used in the management of spinal fractures, spinal canal stenosis, segmental instability, and post-traumatic kyphotic deformities [2]. Spinal fusion has been shown to reduce pain, improve neurological outcomes, and restore spinal stability [3]. The reported

incidence of traumatic spinal injuries ranges from 20 to 70 cases per 100,000 population annually [4]. In the United States alone, approximately 500,000 spinal fusion procedures are performed each year for various spinal conditions [5].

Traditionally, the gold standard for achieving spinal fusion has been autologous bone graft harvested from the iliac crest [6]. However, autograft use is associated with a substantial rate of donor-site complications [7]. These limitations have driven the search for alternative strategies aimed at improving fusion outcomes [8]. Various metal, ceramic, polymeric, and composite biomaterials are currently being investigated as tissue-engineering scaffolds for bone regeneration [9].

Despite advances in implant design and fixation techniques, the incidence of pseudoarthrosis remains high, ranging from 13% to 41.4% [10]. The limited osteoinductive capacity of synthetic implants, which primarily provide mechanical support and osteoconduction, highlights the critical role of biological and cellular regenerative mechanisms in achieving solid fusion [6]. Consequently, interest in cell-based therapies has increased considerably in recent years. Owing to their ability to undergo osteogenic differentiation, secrete angiogenic and growth factors, and modulate the local tissue microenvironment, these approaches promote bone remodeling and regeneration [11].

The aim of this review is to analyse and synthesise current evidence regarding the regenerative potential, clinical efficacy, and safety of cell-based therapies used to enhance osteogenesis in spinal fusion.

2. Materials and methods

A literature search was performed using the PubMed, Web of Science, and Google Scholar databases. Publications published between January 2016 and December 2025 were considered eligible for inclusion.

The following keywords and their combinations were used to identify relevant studies: «thoracic and lumbar spine», «spinal fusion», «mesenchymal stromal cells», «bone morphogenetic protein», «stromal vascular fraction», «bone marrow aspirate» and «cell-based therapies».

Eligible studies included original clinical investigations, randomized controlled trials, systematic reviews, and meta-analyses evaluating the application of cell-based approaches in thoracic and lumbar spinal fusion. Particular attention was given to studies assessing regenerative potential, fusion outcomes, and safety profiles.

Review articles without original data, case reports, letters to the editor, and studies unrelated to biological or cellular augmentation in spinal fusion were excluded. Publications lacking adequate methodological description or clinical outcome reporting, as well as purely experimental studies without clinical relevance, were also excluded from the analysis.

3. Results

Successful spinal fusion requires graft materials possessing osteogenic, osteoinductive, and osteoconductive properties [12]. Osteoconduction refers to the ability of a scaffold to provide a structural framework that supports bone ingrowth, whereas osteoinduction involves the stimulation of osteogenic cell differentiation mediated by bioactive factors [13]. Osteogenesis represents the formation of new bone through the differentiation of osteoprogenitor cells [14]. The combination of cell-based therapies with carrier graft materials represents a promising tissue-engineering strategy aimed at enhancing bone regeneration and improving fusion outcomes [15].

Mesenchymal stromal cells (MSCs)

In 1966, Friedenstein et al. first described mesenchymal stromal cells (MSCs) as fibroblast-like bone marrow–derived cells capable of ectopic osteogenesis, establishing their role as osteogenic progenitors [16]. MSCs are multipotent cells with the capacity to differentiate into several mesodermal lineages, including bone, cartilage, adipose, and tendon tissues [17]. The primary clinical sources of MSCs include bone marrow, adipose tissue, and umbilical cord blood [13]. Bone marrow remains the most commonly used source; however, its harvest requires invasive procedures associated with donor-site morbidity and infection risk [7]. Adipose tissue has therefore emerged as an attractive alternative, as its procurement is less invasive and yields substantially higher numbers of MSC progenitors compared with equivalent volumes of bone marrow [18]. The therapeutic effects of MSCs are largely mediated by their paracrine activity and stromal support functions, involving the secretion of bioactive molecules that regulate tissue repair [18,19]. Through osteogenic differentiation, secretion of angiogenic and growth factors, and modulation of the local microenvironment, MSCs play a central role in bone remodeling and regeneration [11].

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Spinal fracture models have demonstrated the potential advantages of MSC-based constructs [20]. The use of porous titanium scaffolds combined with MSCs has been associated with enhanced bone formation and improved osseointegration compared with cell-free scaffolds. Similar findings have been reported with strontium-modified hydroxyapatite combined with adipose-derived MSCs [20].

A prospective clinical study by Gomez-Ruiz et al. (2023) demonstrated a favourable safety profile of MSC application in lumbar spinal fusion. The study included 11 patients with a mean follow-up period of 10 years. No cases of tumor formation, infectious complications, inflammatory reactions, or heterotopic ossification were reported during the follow-up period [21].

Comparable findings were reported in a clinical study by Blanco et al. (2019), which evaluated the safety and efficacy of MSCs in lumbar spinal fusion. The study included 11 patients with a follow-up period exceeding five years, with successful fusion achieved in 81% of cases [22].

In another clinical study involving 73 patients, García de Frutos et al. (2020) reported earlier and more pronounced fusion at 12 months following MSC application [23].

Bone marrow aspirate (BMA)

Bone marrow aspirate (BMA) is a biologically active graft containing MSCs and growth factors, including BMP-2 and BMP-7, which can confer osteogenic and osteoinductive properties to osteoconductive scaffolds [24]. The osteoinductive potential of BMA is attributed to the release of cytokines and growth factors produced by cellular components within the aspirate [25]. BMA is typically harvested from the iliac crest using a minimally invasive technique [26].

A prospective study involving 10 patients demonstrated that the vertebral body may also serve as an alternative source of BMA. The aspirate obtained intraoperatively formed a natural clot that was applied to the spinal fusion site, creating a biologically active environment favorable for successful fusion [27].

Clinical evidence suggests that the effectiveness of BMA may be influenced by patient age. One study reported fusion rates of 35.7% in patients older than 65 years compared with 76.4% in younger patients [28].

Several clinical investigations evaluating BMA in lumbar spinal fusion have demonstrated consistently high fusion rates [10,24,29,30].

In a prospective study by Chatterjee et al. (2020) involving 42 patients, solid fusion was achieved in all cases within three months following spinal fusion using BMA [29]. Similarly, Noh et al. (2021) reported a fusion rate of 92.8% in a cohort of 150 patients treated with concentrated bone marrow aspirate (cBMA) combined with autograft, allograft, and demineralized bone matrix (DBM) during a follow-up period of up to 24 months [10]. Ajiboye et al. (2016) observed successful fusion in 92.5% of 80 patients treated with cBMA in combination with DBM at 12 months of follow-up [24]. Comparable outcomes were reported by Robbins et al. (2017), who achieved a 91% fusion rate at 12 months using autologous bone graft combined with BMA and nanohydroxyapatite in 46 patients [30].

Stromal-vascular fraction (SVF)

The stromal vascular fraction (SVF) derived from adipose tissue following enzymatic processing of lipoaspirate represents a rich source of regenerative cells and bioactive factors [31]. SVF is a heterogeneous cell population comprising mesenchymal stromal, endothelial, and perivascular cells, as well as fibroblasts and immune cells, and is enriched with growth factors and cytokines [32]. Its regenerative effects are primarily mediated through paracrine signaling, promotion of angiogenesis, immunomodulatory activity, and the contribution of progenitor cells to tissue repair processes [33]. Available clinical evidence suggests that SVF application in spinal fusion demonstrates promising regenerative potential with a favourable safety profile [2,34].

A prospective clinical study by Kim et al. (2020) reported favourable safety outcomes and promising efficacy of SVF application in lumbar spinal fusion in a cohort of 10 patients. The combination of SVF with β-tricalcium phosphate and interbody PEEK cages resulted in successful fusion in all patients at 12 months of follow-up [2].

Comparable findings were reported in a clinical study published in 2025, in which SVF incorporated into a biocomposite hydrogel during interbody cage implantation achieved a fusion rate of 90% in 30 patients after 12 months of follow-up [34].

Bone morphogenetic proteins (BMP)

Bone morphogenetic proteins (BMPs) are members of the transforming growth factor-β (TGF-β) superfamily and play a central role in bone formation and regeneration [35]. BMPs were first described by Urist in 1965 as biological factors capable of inducing ectopic bone formation [36]. To date, approximately 20 BMP subtypes have been identified, among which BMP-2, BMP-4, BMP-5, BMP-6, BMP-7, and BMP-9 are considered key regulators of osteogenesis [37].

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BMP-2 promotes osteogenic differentiation of mesenchymal cells, upregulates osteogenic gene expression, and initiates endochondral ossification [38,39], whereas BMP-7 supports osteoblast maturation and enhances fracture healing [40]. In current clinical practice, recombinant human BMP-2 (rhBMP-2) is the most widely used form, as regulatory approval for BMP-7 has been withdrawn in several countries [41].

A large meta-analysis by Yang et al. (2024), including 39 cohort studies and 7,145 patients, demonstrated significantly higher fusion rates associated with BMP-2 use, whereas the absence of BMP-2 increased the risk of nonunion more than fourfold [5]. A network meta-analysis and systematic review of 43 randomized controlled trials conducted by Ambrosio et al. (2025) further confirmed that rhBMP-2 achieved superior fusion outcomes and lower complication rates compared with autograft [8].

In a retrospective study of 93 patients, Graillon et al. (2016) reported a 100% fusion rate following rhBMP-2 application in combination with interbody cages, without procedure-specific complications at a mean follow-up of 22 months [42].

Similarly, a large prospective clinical study by Scott-Young et al. (2024), involving 1,335 patients with 12 months of follow-up, demonstrated high fusion success when rhBMP-2 was used in combination with structural allograft and PEEK cages [43].

Despite its strong osteoinductive properties, rhBMP-2 use may be associated with adverse events, including radiculitis, heterotopic ossification, transient bone resorption, seroma or hematoma formation, and soft tissue edema, underscoring the importance of strict adherence to dosing and application protocols [39,44,45].

Table 1 - Clinical outcomes of cell-based and biologic technologies in spinal fusion

Studies	Number of patients included in the study	Follow-up period	Method of cell application	Fusion rate
Gomez-Ruiz et al. (21)	11	10 years	MSCs + tricalcium phosphate scaffold	100%
Blanco et al. (22)	11	5 years	MSCs + tricalcium phosphate scaffold	80%
García de Frutos et al. (23)	65	12 months	MSCs + allograft	92,3%
Chatterjee et al. (42)	42	3 months	BMA + interbody implant	100%
Noh et al.(10)	150	24 months	BMA + autograft, allograft, and DBM	92.8%
Ajiboye et al. (24)	80	12 months	BMA + DBM	92,5%
Robbins et al.(30)	46	12 months	BMA and nanohydroxyapatite	91%
Salamanna et al. (27)	10	12 months	BMA clot + posterior lumbar fusion	100%
Kim et al.(2)	10	12 months	SVF + β-tricalcium phosphate + PEEK cage	>90%
Baidarbekov et al. (34)	30	12 months	SVF/biocomposite hydrogel + interbody cage	90%
Graillon et al. (42)	93	22 months	rhBMP-2 + interbody cage	100%
Scott-Young et al.(43)	1,335	12 months	rhBMP-2 + allograft + PEEK cage	99.6%
Sathe et al.(49)	140	12 months	ABM/P-15 + interbody cage	97,9%
Andresen et al.(50)	101	10 years	ABM/P-15 + local bone (non-instrumented fusion)	50%

Bioactive peptides

Bioactive peptides are short amino acid sequences derived from functional domains of proteins that can modulate cellular mechanisms involved in tissue regeneration [46]. Experimental and clinical studies suggest that bioactive peptides promote osteogenesis by enhancing cell proliferation, adhesion, differentiation, and bone matrix mineralization [47]. Among them, the synthetic peptide P-15 is one of the most extensively studied and demonstrates biological activity when adsorbed onto calcium phosphate–based carriers or incorporated into hydrogel matrices [48].

In a retrospective clinical study by Sathe et al. (2022) involving 140 patients, the use of the ABM/P-15 peptide was associated with earlier fusion compared with rhBMP-2 and DBM [49].

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Similarly, Andresen et al. (2025) reported improved fusion outcomes with ABM/P-15 compared with allograft in a cohort of 101 patients followed for 10 years [50].

A systematic review by Hasan et al. (2024) further suggested that ABM/P-15 may promote earlier fusion in lumbar spinal fusion procedures compared with conventional graft materials [51].

Autologous growth factors

Among the most extensively studied growth factors are platelet-derived growth factor (PDGF) and transforming growth factor-β (TGF-β). These factors are obtained through platelet concentration techniques and can be combined with autografts, allografts, or ceramic scaffolds to enhance the likelihood of successful spinal fusion [52]. In bone regeneration, PDGF - particularly the PDGF-BB isoform - stimulates progenitor cell migration and angiogenesis, thereby creating a favorable microenvironment for bone formation and supporting osteogenic activity in synergy with other growth factors [53].

Three isoforms of TGF-β - TGF-β1, TGF-β2, and TGF- β3 - are involved in key biological processes, including inflammation, skeletal development, tumor biology, and bone metabolism [37]. During bone regeneration, TGF- β promotes the recruitment of mesenchymal stem cells to the implantation site and regulates the early stages of osteogenic differentiation [54]. The most common clinical method for delivering these growth factors is platelet-rich plasma (PRP), which serves as a concentrated autologous source of biologically active molecules [55].

Evidence regarding the impact of PRP on spinal fusion outcomes remains inconsistent [56]. Prospective studies have suggested that PRP with high platelet concentrations may enhance early bone regeneration and accelerate initial bone formation following spinal fusion. However, clinically relevant effects were observed primarily when growth factor concentrations exceeded peripheral blood levels by more than fivefold [57].

A meta-analysis by Muthu et al. (2022) reported limited clinical efficacy of PRP in spinal fusion. The use of PRP was not associated with significant improvements in pain outcomes and did not result in higher fusion rates compared with conventional grafting techniques [10].

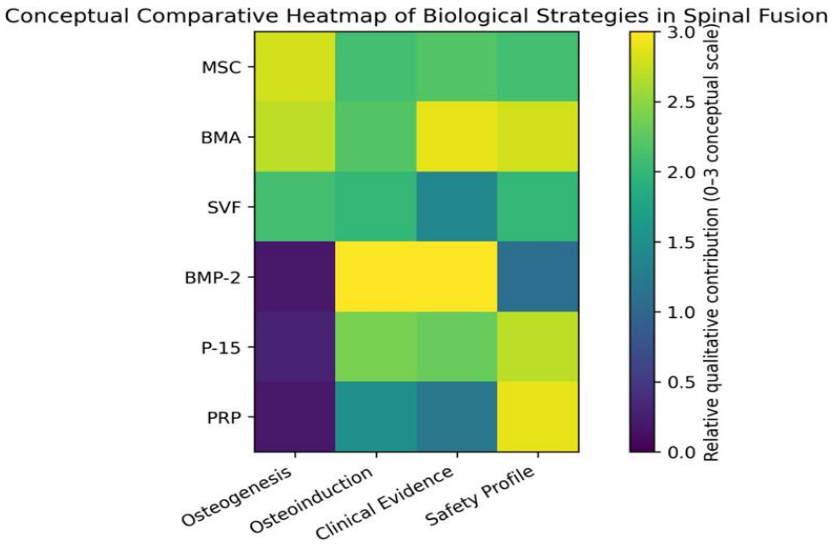

Figure 1 - Comparative heat map of cell-based therapies in spinal fusion illustrating their osteointegration potential, level of clinical evidence, and safety profile

4. Discussion

A review of the available literature suggests that cell-based therapies may enhance spinal fusion by promoting bone repair and regenerative processes. Several clinical studies report favourable safety profiles of MSCs and indicate their potential to improve fusion outcomes and functional recovery [2,23,29]. Among currently available biological agents, BMP demonstrate the most pronounced fusion-enhancing effect [8,42,43]; however, their use is associated with a risk of complications, highlighting the importance of strict adherence to clinical indications and application protocols [39,44,45]. Synthetic peptides facilitate osteogenic cell attachment to graft materials and support extracellular matrix formation, thereby promoting bone formation at the fusion site [13,49,50].

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At the same time, the clinical effectiveness of PRP remains inconsistent, largely due to variability in preparation and application protocols [10,56,57]. Future studies should focus on standardizing protocols for the application of cell-based technologies and evaluating long-term clinical outcomes.

5. Conclusions

Cell-based technologies represent a modern approach to improving the effectiveness of spinal fusion by stimulating osteogenesis and enhancing bone regeneration processes. Research findings demonstrate the therapeutic safety of cell-based technologies and their ability to improve clinical outcomes of spinal fusion. The combined application of biomaterials, cell-based technologies, and osteoinductive adjuvants promotes the formation of stable spinal bone fusion. Future studies should focus on standardizing protocols for the application of cell-based technologies, optimizing tissue-engineered constructs, and evaluating their long-term safety and efficacy.

Conflict of Interest. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Вертебрологияда қолданылатын жасушалық технологияларға салыстырмалы талдау

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Түйіндеме

Омыртқа спондилодезі омыртқа зақымдануларын емдеудің ең кең таралған әдістерінің бірі болып табылады, алайда имплантациялық конструкциялардың жетілдірілуіне қарамастан, жалған буынның (псевдоартроздың) даму жиілігі жоғары деңгейде сақталуда. Осыған байланысты остеогенезді күшейтуге бағытталған жасушалық технологияларға қызығушылық артып келеді. Әдебиеттерді іздеу PubMed, Web of Science және Google Scholar дерекқорларында 2016 - 2025 жылдар аралығында жүргізілді. Талдауға кеуде және бел омыртқасы деңгейінде спондилодез кезінде жасушалық технологияларды қолдануға арналған клиникалық зерттеулер, жүйелі шолулар және метаанализдер енгізілді. Шолуда мезенхималық дің жасушаларын, сүйек кемігінің аспиратын, стромальды-васкулярлық фракцияны, сүйек морфогенетикалық ақуыздарын, биоактивті пептидтерді және аутологиялық өсу факторларын қолдану қарастырылды. Әдебиеттерді талдау жасушалық технологияларды қолдану омыртқаның сүйектік бітісуі кезінде регенеративтік үдерістерді күшейтіп, емдеудің клиникалық нәтижелерін жақсартатынын көрсетеді. Жасушалық технологиялар омыртқаның сүйектік бітісу тиімділігін арттырудың перспективалы бағыты болып табылады. Болашақ зерттеулер жасушалық технологияларды қолдану хаттамаларын стандарттауға және емдеудің ұзақ мерзімді нәтижелерін зерттеуге бағытталуы тиіс.

Түйін сөздер: кеуде және бел омыртқа бөлімдері, спондилодез, мезенхималық дің жасушалары, сүйек морфогенетикалық ақуызы, стромальды-васкулярлық фракция, сүйек кемігінің аспираты, жасушалық технологиялар.

Сравнительный анализ клеточных технологий, применяемых в вертебрологии

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Резюме

Спондилодез является одним из наиболее распространенных методов лечения повреждений позвоночника, однако, несмотря на совершенствование имплантационных конструкций, частота псевдоартроза остается высокой. В связи с этим возрастает интерес к клеточным технологиям, направленным на усиление остеогенеза. Поиск литературы проводился в базах данных PubMed, Web of Science и Google Scholar за период 2016–2025 гг. В анализ включались клинические исследования, систематические обзоры и метаанализы, посвященные применению клеточных технологий при спондилодезе грудного и поясничного отделов позвоночника. В обзоре рассмотрено применение мезенхимальных стромальных клеток, аспирата костного мозга, стромально-васкулярной фракции, костных морфогенетических белков, биоактивных пептидов и аутологичных факторов роста. Анализ литературы показывает, что применение клеточных технологий способствует усилению регенеративных процессов при костном сращении позвоночника и улучшению клинических результатов лечения. Клеточные технологии представляют перспективное направление повышения эффективности костного сращения позвоночника. Дальнейшие исследования должны быть направлены на стандартизацию протоколов применения и изучение долгосрочных результатов лечения.

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Ключевые слова: грудной и поясничный отделы позвоночника, спондилодез, мезенхимальные стволовые клетки, костный морфогенетический белок, стромально-васкулярная фракция, аспират костного мозг, клеточные технологий.

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