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RECENT ADVANCES IN ORTHOPEDIC MANAGEMENT OF JOINT AND SPINE DISORDERS: CURRENT EVIDENCE AND FUTURE PERSPECTIVES

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ABSTRACT
Joint and spine disorders are among the leading causes of chronic pain, disability, and reduced quality of life worldwide, creating substantial clinical and socioeconomic challenges. Continuous advances in orthopedic science have transformed the management of these conditions through the integration of precision medicine, digital technologies, minimally invasive procedures, and regenerative therapies. This review provides a comprehensive overview of recent developments in the orthopedic management of joint and spine disorders, emphasizing current evidence and future perspectives. It discusses the underlying pathophysiological mechanisms, emerging diagnostic approaches based on advanced imaging, artificial intelligence, wearable technologies, and precision biomarkers, as well as contemporary non-surgical and surgical treatment strategies. Recent progress in robotic-assisted surgery, computer-assisted navigation, three-dimensional printing, stem cell therapy, platelet-rich plasma, gene therapy, biomaterials, and tissue engineering is also critically examined. In addition, the review highlights the growing contribution of artificial intelligence and precision medicine in supporting personalized clinical decision-making and improving patient outcomes. Although these innovations have demonstrated considerable promise, important challenges remain, including limited long-term clinical evidence, lack of standardized treatment protocols, high implementation costs, and regulatory considerations. Future research should prioritize multidisciplinary collaboration, large-scale clinical trials, and the integration of emerging technologies to establish evidence-based, patient-centered orthopedic care. Collectively, these advances are expected to enhance diagnostic accuracy, optimize therapeutic outcomes, and reduce the global burden of joint and spine disorders.

KEYWORDS: Joint disorders, Spine disorders, Precision orthopedics, Regenerative medicine, Artificial intelligence.

1. INTRODUCTION

Joint and spinal musculoskeletal disorders are one of the most common causes of chronic pain, functional disability and decreased quality of life globally. These are very closely related to demographic changes, such as an increase in life expectancy, ageing populations and sedentary lifestyle, obesity and the increase in prevalence of chronic metabolic diseases. As a result of the aging of population, degenerative joint disease, spine disease and associated disabilities will be a greater burden than ever before in the healthcare systems and there is a demand for better and sustainable orthopedic management strategies [1].

Orthopedic diseases affect not only the health of individuals, but also have important socioeconomic implications. Musculoskeletal disorders (MSDs) are an important contributor to years lived with disability (YLDs) and disability adjusted life years (DALYs), an indicator of the burden of a health problem in terms of productivity and health care costs [2]. DALYs have been adopted as a common measure, which has been useful in assessing the burden of disease across a wide variety of health conditions and prioritising health care resources and policy making based on evidence [3,4]. Such epidemiological trends make a compelling case for novel methods to reduce the burden of these joint and spine problems in long-term patients as well as to improve outcomes.

In the past decade, there have been amazing developments in the area of orthopedic practice. The traditional approach to management used to be either conservative or an open surgical approach to correct the deformity. In recent years, however, progress has been made towards precision medicine, minimally-invasive methods, biologically targeted treatments and digitally integrated, patient-centred care paths. With the vast amount of large-scale clinical data, real-time patient monitoring and advanced computational technologies, personalized treatment strategies that optimize clinical decision making and postoperative recovery are being developed at an accelerating pace [5].

Accompanying progress in biomedical engineering has further complemented the therapeutic approaches for orthopedic disorders. New technology like robotic surgery, computer-assisted surgery (C.A.S.), three dimensional (3D) printing, regenerative medicine, stem cell therapy, biologic injections and tissue engineering are changing the way complex joint and spine conditions are managed. All these together are intended for the purpose of not just restoring anatomical function, but also to create a biological healing environment, minimise complications, and improve long-term functional outcomes [6]. Furthermore, the role of interdisciplinary integration between orthopedic surgeons, bioengineers, rehabilitation experts and data scientists is becoming increasingly crucial in the process of transferring new technologies to the standard clinical workflow [7].

Artificial Intelligence (AI) is also one of the revolutions in modern orthopaedic practice. In recent years, machine learning algorithms have been gaining popularity for their use in diagnostic imaging, preoperative surgical planning, implant customization, prediction of post-surgery results and surgical outcome monitoring. These technological tools can help to improve diagnostic processes, treatment plan customization, evidence-based clinical decision making and health care efficiency [8].

In the rapidly developing field of orthopedics science, a comprehensive synthesis of the latest evidence becomes essential and timely. The present review critically evaluates the latest advances in orthopedic treatment of joint and spine diseases that include advancements in diagnostics, conservative and surgical treatment, regenerative medicine, digital technology and artificial intelligence. It also highlights the existing problems in the field, as well as opportunities of knowledge advancement for the development of future orthopedics. The following are the research objectives of the study:

- Summarize recent advances in orthopedic management.
- Evaluate current evidence for joint and spine disorders.
- Highlight future research directions.

2. Pathophysiology and Disease Mechanisms

Age, genes, inflammation, and mechanical stress in the process of tissue repair are all factors that cause joint and spine disorders. These are not simply isolated structural abnormalities but rather consist of progressive changes in the cartilage, the subchondral bone, the IV discs, the ligaments, synovium and associated musculature. There have been tremendous advances in recent years in understanding these biological processes and the opportunity now exists to target therapeutic strategies at the mechanisms underlying tissue degeneration as opposed to just addressing the symptoms of the problem [9].

The degenerative joint diseases are a family of diseases that all have the common characteristic of progressive loss of the articular cartilage and remodeling of the subchondral bone, with chronic synovial inflammation in the case of osteoarthritis. Mechanical overload, oxidative stress and inflammatory mediators lead to the release of cytokines, and matrix-degrading enzymes like matrix metalloproteinases and aggrecanases, which further increase ECM degradation. With the progressive degradation of cartilage, there is a change in biomechanics of the joint and joint pain, decreased movement, and loss of joint functionality. The objective of regenerative medicine is to block the cascade and regenerate the degenerated tissue using biologically active interventions like biomaterials, growth factors, and stem cells [10].

The use of artificial intelligence (AI) and machine learning has expanded the knowledge of the disease mechanisms by enabling the analysis of complex biological data and identification of patterns hitherto unnoticed and linked to tissue degeneration. Genomic, proteomic and imaging and clinical data can be used in predictive algorithms to stratify disease phenotypes, and give an individual risk of disease progression and help individualise treatment planning. Computer-assisted technologies play an important role in making general management methods more precise and creating regenerative orthopedics, which can be personalized according to each patient's biological peculiarities and specificities of his/her disease.

Also, an extremely important role is played by bone remodeling in orthopedic diseases. The formation of bones by osteoblasts and bone resorption by osteoclasts is a very intensive process that occurs in the human body and is necessary for the maintenance of healthy bones. This process is affected by various conditions, such as aging, chronic inflammation, hormonal imbalance and metabolic disorders, which cause poor bone quality, slow bone healing, and increased susceptibility to joint and spinal degeneration. As far as the field of orthopedics is concerned, recently there have been some trends towards the introduction of artificial intelligence-assisted decision-making in the area of bone health assessment, bone fracture risk prediction, selection of implants, and postoperative monitoring.. These technologies can help to make better decisions based on patient-specific factors and evidence from the clinical setting [11].

Intervertebral disc degeneration is one of the main biological mechanisms involved in chronic low back pain, and is one of the more frequent spinal conditions. As we age, the intervertebral disc becomes less cellular, low in proteoglycan, and less able to retain water, resulting in loss of intervertebral disc height and mechanical resilience. Degenerated discs have an increased production of inflammatory cytokines, degradation of the extracellular matrix, cellular senescence and disruption of the structure of the annulus fibrosus and nucleus pulposus. This may then lead to a progressive loss of integrity, resulting in facet joint degeneration, nerve impingement and chronic pain. Multiple factors such as mechanical loading, oxidative stress, disruption in nutrient transport, genetic predisposition and immune mediated inflammatory response have been suggested as underlying these pathological processes and are currently being investigated [12].

The cellular level involves the cells that are used as potential mediators for tissue regeneration using the mesenchymal stem cells (MSCs) that possess anti-inflammatory, anti-apoptotic and immunomodulatory properties. Exosomes from the MSCs have attracted considerable attention due to their ability to transport proteins, lipids, mRNA and miRNA between cells. Paracrine effects of the exosomes, including the reduction of oxidative stress, inhibition of apoptosis, and stimulation of tissue repair have been demonstrated in experimental researches and could potentially be used in the regeneration of cartilage, bone and intervertebral discs [13].

It is very important to identify reliable biomarkers to understand the progression of diseases and personalized medicine. Nevertheless, the development of imaging analytics enables creating the foundation AI models that could be used to get quantitative imaging biomarkers that will not be limited by the radiological interpretation only. These backbone models were created based on the training in oncology, but they have great potential for the application in orthopedics, e.g. in automated tissue characterization, disease progression, treatment response and personalized risk stratification. The incorporation of molecular and clinical data would result in improved accuracy in diagnostics and a more targeted treatment approach for joint and spine diseases [14]. The biological pathways that play an essential role in the pathogenesis of joint and spine disease include inflammatory, degenerative, cellular, and biomarker pathways as outlined in Table 1 below.

Table 1. Key pathophysiological mechanisms in joint and spine disorders

Mechanism	Main tissue involved	Pathological process	Clinical relevance	Sources
Cartilage degeneration	Articular cartilage	Matrix breakdown, chondrocyte dysfunction, inflammatory mediator release	Pain, stiffness, reduced mobility	[9]
AI-defined disease phenotyping	Multitissue datasets	Integration of imaging, genomic, and clinical data	Supports risk prediction and precision care	[10,11]
Disc degeneration	Intervertebral disc	Loss of proteoglycans, reduced hydration, annular disruption	Low back pain, instability, nerve compression	[12]
Oxidative stress and exosome signaling	Stem cell microenvironment	MSC-derived exosomes reduce oxidative damage and apoptosis	Potential role in tissue repair	[13]
Imaging biomarkers	Musculoskeletal imaging data	Quantitative tissue characterization using advanced models	Disease staging and outcome prediction	[14]

3. Advances in Diagnostic Approaches

The correct and timely diagnosis is the foundation of good orthopedic treatment; in particular the pathological changes in the complex joint and spine disease may be noticed before clinical symptoms. In recent years, technological advances have greatly facilitated the detection of structural abnormalities, the characterization of the integrity of tissues and, to a certain extent, the prediction of disease progression. With the current diagnostic paradigm, sophisticated imaging, artificial intelligence (AI), and wearable and precision diagnostics are being increasingly used for complete evaluation of patients and for personalized care strategies [15].

In the field of orthopedics, medical imaging is still the most important method for diagnosis. Although conventional radiography is still the main modality for assessment of fracture and joint alignment and of degenerative changes, the sensitivity of conventional radiography for early cartilage and soft tissue changes is low. Modern imaging methods such as high-resolution magnetic resonance imaging (MRI), computed tomography (CT), ultrasonography and hybrid imaging methods are far better at imaging cartilage, ligaments, tendons, inter vertebral discs and surrounding soft tissues. Functional and quantitative imaging also allows for more accurate assessment of tissue composition, biomechanics and early degenerative changes, prior to the development of irreversible structural changes, to aid in diagnosis and treatment planning.

AI has proven to be a valuable addition to diagnostic imaging techniques, improving the interpretation of medical images and minimizing the variability among different observers. Machine learning and deep learning algorithms are able to automatically recognize anatomical structures, characterize subtle pathological features, quantify the extent of the disease and help clinicians to discriminate between normal aging and pathological degeneration. Additionally, AI-powered image analysis can streamline workflows and enable uniform reporting of results, which fosters greater consistency in clinical decision-making processes. With the constant improvement of computational models, AI is projected to be a key part of the orthopedic diagnostic pathway [16].

In addition to diagnostics in the clinic, the technology of wearables has created more opportunities for continuous monitoring of patients. Objective assessment of gait, joint mobility, balance, physical activity and postoperative functional recovery can be assessed by smart wearable devices that are equipped with accelerometers, gyroscopes, and motion sensors. After total knee arthroplasty (TKA), clinicians can use remote patient monitoring to monitor rehabilitation progress in real time and decrease the number of outpatient visits. Functional data can be collected continuously and thus help identify complications or delayed recovery in an early stage, which then enables timely clinical intervention and individual rehabilitation programs [17].

Another important milestone in the treatment of orthopedic conditions is precision diagnostics. Precision diagnostics based on molecular biomarkers, genetic information, biochemical profiles and advanced imaging characteristics provide disease phenotypes at the individual level, as opposed to traditional diagnostics, which are mostly based on clinical examination and imaging characteristics. This is a multi-dimensional approach that helps to increase the specificity of diagnosis, risk stratification and personalized therapeutic decision making. In the near future, the early diagnosis of degenerative joint and spine diseases will become even more promising with the use of molecular biology tools, in conjunction with computational analysis [18].

In recent years, the clinical evidence has also highlighted the worldwide relevance of precision diagnostic approach to improve the efficiency in healthcare. Cost-effective personalized diagnostic pathways have been shown in comparative studies to lead to fewer unnecessary investigations, better use of resources and better clinical outcomes. Although much of this evidence is in other medical specialties, the principles are becoming, and should become, more and more applied to musculoskeletal care, with an increasing amount of precision medicine becoming integrated into orthopedic care [19]. Other examples of the ongoing trend of making faster, more accurate and more personalized assessment of disease include continued innovations in diagnostic technologies like highly sensitive molecular detection systems, and new methods for visualizing signals. These developments will work with imaging- and AI-assisted diagnosis and enable earlier intervention and more focused management approaches in patients with joint and spine diseases [20]. In orthopedic diagnostics, the modern diagnostic pathway will incorporate the latest imaging technologies, AI, wearable devices and precision biomarkers for personalized decision making as illustrated in Figure 1.

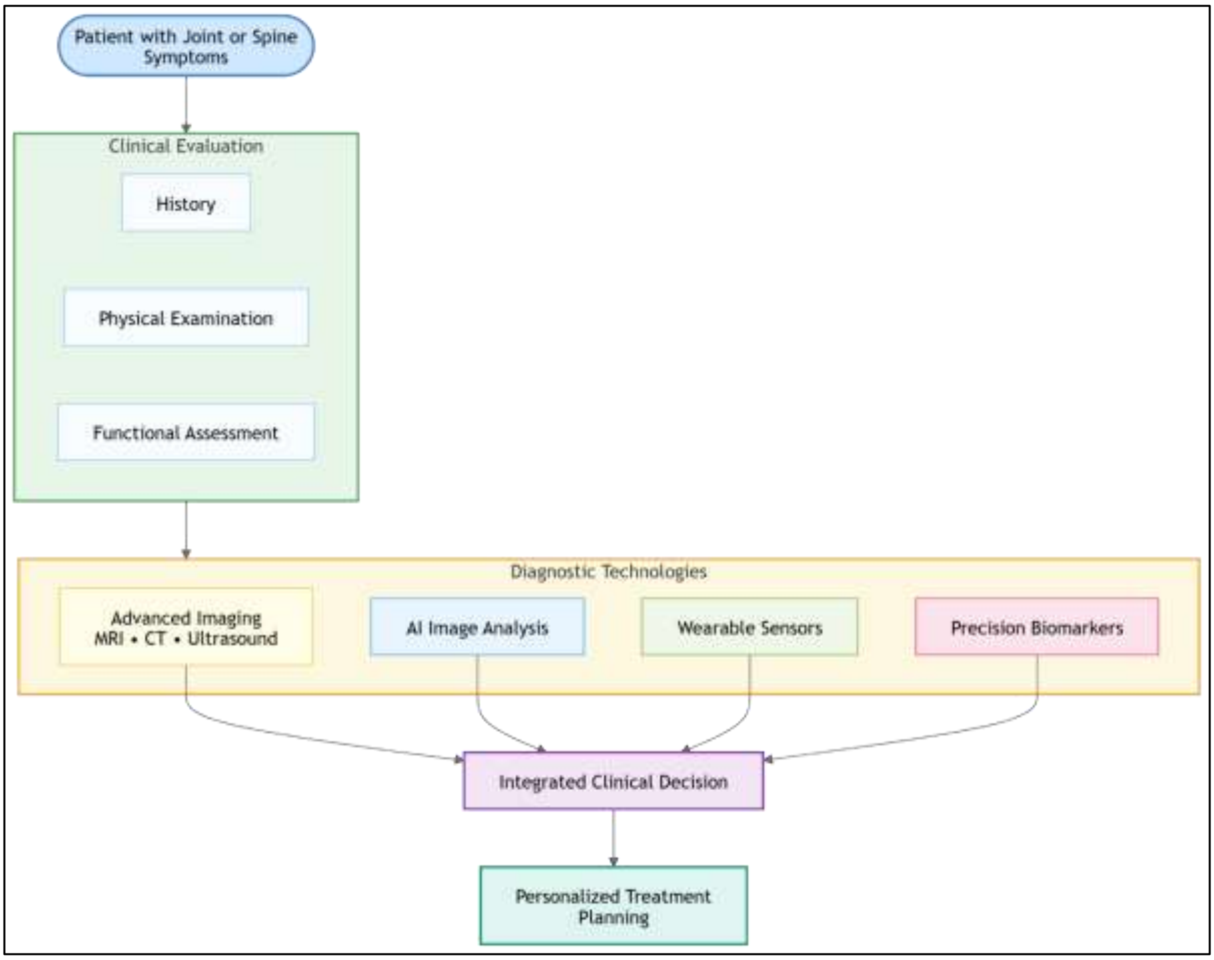

Figure 1. Integrated precision diagnostic workflow for joint and spine disorders

4. Contemporary Non-Surgical Management

Most joint and spine conditions will be treated first with conservative (non-surgical) therapy, with a goal of improving patients' quality of life, slowing the disease process, and improving joint function while relieving pain. In recent years, treatment has evolved from a general symptomatic to precision-based patient-centred treatment, and includes a combination of pharmacological treatments, rehabilitative measures, minimally invasive interventions and lifestyle changes. It is a multidisciplinary approach that considers the biological and functional diversity of musculoskeletal disorders and the necessity of individual treatment, depending on the severity of the disease, the characteristics of a patient and the clinical response to the treatment [21].

The potential for the use of pharmaceutical treatments of degenerative and inflammatory joint conditions has been greatly expanded. New drugs in the development for OA are more and more geared toward the molecular mechanisms involved in cartilage destruction, inflammation and inappropriately altered bone remodeling, rather than pain alleviation. Precision medicine strategies like the utilization of disease markers and personalized risk scores have enabled the provision of treatment options which could alter the course of the disease in favor of patients. Similarly, the treatment of rheumatoid arthritis has undergone several changes since new drug targets have emerged and they are associated with immunity and inflammation pathways. With the emergence of biologics and small molecule inhibitors, control over rheumatoid arthritis has become better and structural joint damage has decreased as well [22].

Orthopedic conservative therapy remains an important component of the rehabilitation process. Rehabilitation nowadays focuses on the patient, on restoring his or her functionality, and using a teamwork approach, which involves orthopedic surgeons, physiotherapists, occupational therapists, and pain management professionals. Patient-specific approaches to rehabilitation include exercises for strengthening, joint stability, mobility, and physical functioning. The value of the patient-specific and multidisciplinary approach to managing complex musculoskeletal problems is illustrated by the efficiency of patient-specific rehabilitation pathways in different chronic neurological diseases [23].

There has also been a revolution in the provision of rehabilitation services due to advances in technology, such as telemedicine and telehealth technologies. Tele-rehabilitation (or telo-rehabilitation) is an integrated system that includes wearable technology for the patients, robotic systems and augmented reality systems to offer home-based rehabilitation, and to monitor remotely the patients' adherence to treatment and recovery process. These tele-rehabilitation technologies increase the accessibility of the rehabilitation services, encourage patients to stay engaged and monitor regularly their therapeutic outcomes, particularly when the patient suffers from mobility problems or lives in far-off places [24].

Image-guided minimally-invasive procedures represent an important aspect of non-surgical management of the orthopedic patient especially when they are poorly controlled by medications and physiotherapy. However, intra-articular corticosteroid and hyaluronic acid injections remain among the most frequently used procedures to alleviate symptoms, and new approaches including platelet-rich plasma injections, genicular nerve blocks, and radiofrequency ablation are also available for alleviation of chronic pain associated with the osteoarthritis. Clinical studies are being conducted to compare the efficacy of these procedures with other treatment options and achieve optimal pain control and functionality and reduce necessity of surgical intervention [25].

The other essential element of all orthopedic treatment is lifestyle changes. The joint degeneration and back pain problems are heavily influenced by excessive body weight, lack of physical exercises, poor nutrition and negative psychological factors. The specific programs based on the physical activity, diet, weight loss and psychological counseling have been proven to increase mobility and diminish pain. These programs are multidisciplinary lifestyle programs which aim to minimize the mechanical stress on weight bearing joints and influence systemic inflammatory processes related to obesity [26]. The current evidence also highlights the importance of combining nutrition and regular exercise as a key component of longterm strategies for obesity-related musculoskeletal disorders as well as to ensure that current medical treatments are most effective [27]. The main non-surgical modalities for the treatment of joint and spine diseases currently available are listed in Table 2 and their therapeutic targets are indicated.

Table 2. Contemporary non-surgical management strategies for joint and spine disorders

Strategy	Main indication	Therapeutic aim	Key advantage	Sources
Precision pharmacotherapy	Osteoarthritis	Targets cartilage degeneration, inflammation, and abnormal remodeling	Moves beyond symptom control	[21]
Targeted anti-inflammatory therapy	Rheumatoid arthritis	Modulates immune and inflammatory pathways	Reduces structural joint damage	[22]
Personalized rehabilitation	Chronic functional impairment	Improves mobility, strength, and independence	Patient-specific recovery pathway	[23]
Telerehabilitation and robotics	Postoperative or long-term rehabilitation	Enables supervised remote therapy	Improves access and monitoring	[24]
Image-guided pain interventions	Knee osteoarthritis pain	Injection, nerve block, or radiofrequency-based pain relief	May delay surgery in selected patients	[25]
Lifestyle intervention	Obesity-related joint and spine burden	Weight control, exercise, diet, mental health support	Reduces mechanical and systemic stress	[26,27]

5. Surgical Advances in Joint and Spine Disorders

In the last decade a lot has changed in the world of surgical management of joint and spine disorders with new technologies that have improved the precision of the procedures, reduced trauma to tissues and improved recovery after surgery. In recent years, orthopedic surgery more and more concentrates on patient-specific treatment approaches, which are supported by modern imaging and computer-supported techniques as well as minimally invasive methods. Such advancements have helped reduce complications, shorten the time required for recovery and improve the outcomes of the procedure in comparison with many traditional surgical techniques [28].

In modern times, minimally invasive orthopedic surgery has become an integral element of treatment for degenerative joint diseases and diseases of the spine. In each case, whether it is the arthroscopy of the joint or minimally-invasive surgery of the spine, it is done through small incisions and specialized equipment that allows preservation of the surrounding soft tissues and effective correction of the disease of the joint or spine. Some of the most important advantages of these techniques are a reduction in blood loss, reduction in post-operative pain, shorter hospital stays and early mobilization. The Enhanced Recovery after Surgery (ERAS) protocols which complement the minimal invasive surgery, for the purposes of improving anesthetic, multi-modal pain treatment, earlier rehabilitation and nutritional support in order to hasten the process and ensure satisfaction.

Robotic assisted surgery is one of the most significant developments within orthopedic surgery. The robotic devices can help the surgeons attain high accuracy in terms of implant placement and positioning, bone preparation, as well as navigation during surgery. The use of such systems increases the accuracy of the surgery, reduces human errors and improves the reproducibility of the procedures. Robotic arms may help in fitting the implant during joint replacement surgery or placing the pedicle screws accurately during spine surgery, and hence prevent any damage to the neurovascular

structures. Though technologically more challenging and costly initially, robotic surgery still holds much promise in terms of improving surgery quality and patient outcomes [29].
The use of robotic systems in spine surgery is rapidly growing in recent years. Based on systematic reviews and meta-analysis of literature, robot-assisted spine surgery has been shown to be associated with more accurate implant positioning, reduced radiation exposure to surgical staff and reduced complications associated with instrumentation as compared to freehand surgery. While the operative times may be longer in the learning phase, with more surgical experience, it has resulted in a more efficient operating time and more consistent clinical outcomes [30]. Multicenter studies have also indicated that as the technology of robots evolves and surgeons become more adept, patients undergoing complex spinal surgery have improved safety rates, complication rates, and postoperative recovery rates.
Computer-assisted navigation has enhanced intraoperative decision making not only by combining real-time imaging with three dimensional anatomy reconstruction but also by providing robotic assistance. Navigation allows better accuracy in implant positioning and it helps in correcting complex deformities accurately and with minimum damage to neighbouring tissues. Together with the robotic platforms, the navigation technologies have resulted in very integrated surgical workflow and increase the precision of the entire surgical process. Current evidence suggests that these technologies will continue to be used more and more to enhance surgery reproducibility, decrease revision surgery, and maximize patient-specific outcome for a myriad of orthopedic surgeries [31].
The use of three-dimensional (3D) printing and virtual surgical planning have also improved with the goal of personalized surgical planning. High-resolution imaging can create patient-specific anatomical models for visualization of difficult deformities, for simulating surgical procedures and improving pre-surgical planning of implants or surgical guides. These technologies are used to aid in the pre-operative planning, to help the communication between different multidisciplinary teams and to aid with the more accurate execution of technically challenging procedures. With the ongoing advancement of additive manufacturing techniques, individualised implants and customised surgical solutions can be predicted to be more and more part of everyday orthopedic practice. Over the past few years, the field of orthopedics has seen significant progress in surgical techniques, moving towards a more “minimally invasive” approach and using robots, surgical navigation, and patient-specific implants, as detailed in Figure 2.

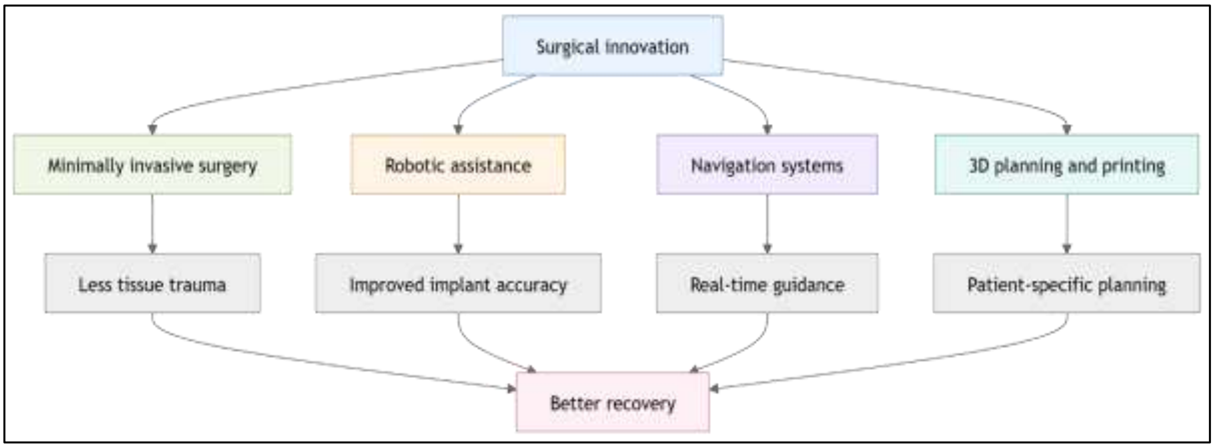

Figure 2. Technology-driven surgical advances in orthopedic care

6. Regenerative Medicine and Biological Therapies

Regenerative medicine has emerged as a transformative approach in orthopedic care that aims to be a biological treatment seeking to address the mechanisms that underlie tissue degeneration instead of merely alleviating symptoms. While traditional therapies are mainly focused on pain relief or restoration of mechanical stability, regenerative therapies aim to repair damaged cartilage, bone, ligaments, tendons and intervertebral discs by means of cellular, molecular and bioengineering strategies. These innovations are significant in terms of potential to slow disease progression, increase functional recovery and to avoid or postpone major reconstructive surgery in some patients [32].
Stem cell therapy is one of the most intensively researched methods of regeneration for musculoskeletal disorders. Mesenchymal stem cells (MSCs) have been shown to be capable of differentiating into several types of connective tissue, and are known to have strong immunomodulatory and anti-inflammatory properties through paracrine effects. More recently, induced pluripotent stem cell derived mesenchymal stem cells (iPSC-MSCs) have been gaining more and more attention in the research field due to its abundant and renewable cell source, which has a decreased donor variability and a greater proliferative capacity. Experimental and early clinical trials indicate that they could be used to enhance cartilage regeneration, speed up bone repair and even help to restore intervertebral discs, but this still needs to be clinically validated for more widespread use.
The use of platelet-rich plasma (PRP) therapy has grown to become a popular biologic treatment in orthopedic practice. PRP is a product made from one's own blood, containing a high number of platelets that release numerous bioactive molecules essential to tissue repair, angiogenesis and controlling inflammation. The clinical data suggest that PRP could be beneficial in the treatment of selected patients with OA, tendinopathies, and ligament injuries and in some soft tissue disorders for their symptomatic improvement. However, various preparation methods, platelet dose and method of delivery continues to influence treatment outcomes and well-defined clinical guidelines and patient selection criteria remain to be established [33].

Growth factors and cytokines are important in tissue regeneration in their role of controlling the proliferation, differentiation, synthesis of extracellular matrix and immune response. The therapeutic effects of these signaling molecules have also been enhanced by the development of biomaterials, nanocarriers and scaffold-based delivery systems, which has facilitated their stability. While encouraging preclinical data is available, key challenges that remain for use in the orthopedic setting include dose optimization, targeting, biologic stability, and scalability to clinical dose.

Another field in orthopedic regeneration, that is still in its infancy, is gene therapy. The aim of gene-based therapies is to stimulate the repair capacity of the tissue in the target cells, block the inflammation signalling or correct the processes in the cells that cause tissue degeneration. Clinical trials of gene therapy are a continually expanding series of experiments, reflecting a rising interest in the use of gene therapy in various disease states with musculoskeletal diseases being targeted as a new therapeutic option. Further studies should focus on improving the safety of the vector and its ability to deliver genes and to treat orthopedic disorders in the long-term [34].

Tissue engineering is a combination of biomaterials, living cells and bioactive molecules to develop a functional biological substitute that can regenerate damaged musculoskeletal tissues. For intervertebral disc degeneration, engineered scaffolds aim to mimic the native matrix and at the same time ensure that cells survive and that tissue is regenerated. New biomaterials, such as injectable hydrogels, biodegradable polymers and composite scaffolds, have paved the way for better mechanical and biological conditions for disc repair. In addition, approaches to mimic the complex disc microenvironment (e.g., manipulation of oxygen tension, nutrient transport, inflammation, and mechanical loading) should also improve outcomes of regenerative therapy and contribute to the generation of precision therapies for spinal degeneration [35, 36]. The main regenerative and biological therapies mentioned in this review are summarized in Table 3 and highlighted in terms of their mechanisms, uses and translational limitations.

Table 3. Regenerative and biological therapies in orthopedic management

Therapy	Biological principle	Potential application	Main limitation	Sources
iPSC-derived MSCs	Cell-based repair and immunomodulation	Cartilage, bone, and disc regeneration	Requires long-term safety validation	[33]
Platelet-rich plasma	Platelet-derived growth factor release	Osteoarthritis, tendinopathy, soft tissue injury	Protocol variability	[34]
Growth factors and cytokines	Regulation of cell proliferation and matrix synthesis	Tissue repair and regenerative signaling	Delivery and dosage challenges	[35]
Gene therapy	Genetic modulation of repair pathways	Inflammation control and tissue regeneration	Vector safety and clinical translation	[36]
Biomaterial scaffolds	Structural support for cell survival and matrix formation	Disc and cartilage repair	Need for mechanical and biological optimization	[37,38]

7. Tissue Engineering and Biomaterial-Based Innovations for Joint and Spine Repair

Tissue Engineering has emerged as a core element of future orthopedics, which uses biomaterials, cells and bioactive small molecules to restore structure and function to damaged musculoskeletal tissues. Tissue engineering is not a traditional reconstructive approach but it is an approach to recreate the native biological environment for long-term tissue regeneration. This is especially important for conditions like cartilage defects and intervertebral disc degeneration, where the ability of native tissues to heal is restricted. However, with the progress in the understanding of cellular microenvironment, regenerative platforms with better environment of tissue repair have been developed to tackle the mechanisms of degeneration [37].

Biocompatible scaffold materials provide structural framework for cell attachment, proliferation, differentiation and extracellular matrix deposition. Modern scaffolds are designed to be similar to the structure and function of the native cartilage and bone and are designed to be metabolized as they are replaced by new tissue. Stem cell survival and cartilage regeneration has been shown to be supported by both natural biomaterials as well as synthetic polymers and hybrid composites. The ability to embed bioactive molecules into these scaffolds further enhances the ability of cells to communicate and to form said organized tissue, thus scaffold-based therapies are becoming an ever more appealing approach in orthopedic regeneration [38].

Scaffold-assisted regeneration has also been found to be a promising technique to be used in complex fibrocartilaginous structures, e.g. the temporomandibular joint (TMJ) disc. Due to the special biomechanical requirements of the TMJ, engineered scaffolds should have sufficient mechanical strength, flexibility, biocompatibility, and promote vascular integration and extracellular matrix remodeling. The focus of recent advances has been the design of multilayered scaffolds, new biomaterials and cell-seeded constructs that mimic the native organization of the joint disc. These strategies have yielded promising preclinical results, and could be used as future alternatives to traditional reconstructive surgery [39].

Tissue engineering utilizing biomaterial (BTE) is a novel strategy for treating disc degenerative disease in spinal disorders. In order to rehydrate the disc along with providing mechanical strength and cell viability, hydrogels, biodegradable polymer, and composite biomaterials are being designed. Precision medicine concepts have also had an impact on scaffold design, allowing for patient-specific anatomical, biological and biomechanical characteristics. Such personalized regenerative platforms could enhance the effectiveness of such an approach and minimize the variability that is commonly seen with traditional therapeutic strategies [40].

It is also important to recreate the complex microenvironment of the damaged tissue in order to achieve successful tissue regeneration. Cell behavior and regeneration capacity are strongly affected by parameters like the availability of oxygen, transport of nutrients, mechanical loading, inflammatory signalling and extracellular matrix composition. Research is thus focused on the development of biomaterials that will actively manipulate these microenvironmental conditions instead of just passively supporting the structure. Next-generation scaffolds will combine controlled growth factor, stem cell and immunomodulatory molecule delivery to hopefully create a more favorable environment for long-lasting tissue regeneration and functional recovery [41].

The future of orthopedic tissue engineering will most likely rely on the ability of biomaterial scientists, cell biologists, bioengineers, and orthopedic surgeons to collaborate in a multidisciplinary fashion. Regenerative outcomes can be expected to increase, and clinical translation rates should speed up with advances in scaffold fabrication techniques such as three dimensional bioprinting, nanotechnology and patient-specific biomaterial design. Further improvements of the scaffold composition, mechanical properties and biological functionality will be important to ensure that tissue-engineered constructs can be reliably used as therapeutic constructs for complex joint and spine disorders [42]. Scaffold design, cell support, bioactive signaling and microenvironmental control are the four foundations of the role of tissue engineering in joint and spine repair (Figure 3).

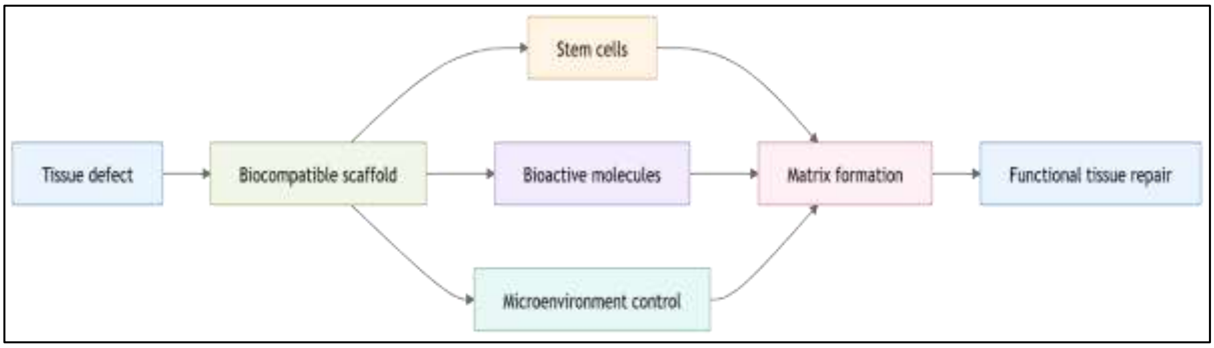

Figure 3. Tissue engineering framework for joint and spine regeneration

8. Present status, problems, and prospects

The current literature suggests that orthopedic care continues to move towards personalized care and away from standard symptom-based treatment. Strong evidence from high quality systematic reviews, meta-analyses and randomized clinical trials now exists to support a variety of minimally invasive procedures, biologic therapies, multidisciplinary rehabilitation and individual treatment pathways. These developments have led to better pain management, functional recovery and patient satisfaction and highlight the need for careful patient selection of interventions tailored to the severity of the disease, patient parameters, and long-term clinical outcomes [43].

However, there are still a few problems that hinder the adoption of new orthopedic technologies. Different treatment protocols, different inclusion criteria for patients, lack of long-term follow-up and differences in clinical outcomes reported make it difficult to compare different studies. While there are many different conservative or surgical options, the sequence of treatments remains unclear, and it is not clear which patients are likely to benefit most from which treatments, especially in the case of knee osteoarthritis [44].

The changes in treatment approaches in other musculoskeletal conditions further emphasize the need for ongoing evidence synthesis and technology development. Recent reviews have shown that surgical outcomes are much improved with improved surgical technique, understanding of the disease mechanisms and care during the perioperative period. But, as with any new technologies, there are important considerations for the balance between innovation, safety, cost of technology, and accessibility to the technology before it can be routinely used in clinical practice [45].

The next steps in orthopedic research should focus on large, multicenter RCTs, standardized outcome measures and long-term follow up to determine the relative effectiveness of new treatments. As AI, Regenerative Medicine, Advanced Biomaterials and Precision Diagnostics gain traction in the field, it is possible to see more personalized treatment algorithms and improved surgical planning and monitoring in the future [46]. With the current rapid transformation in technology, collaborative research efforts between clinicians, biomedical engineers and data scientists will be necessary to transform those advances into clinically-effective and economically viable evidence-based orthopedic care.

9. CONCLUSION

Over the last few years, revolutionary developments in orthopedic management have dramatically changed the way joint and spine diseases are diagnosed and managed from traditional symptom-focused strategies toward precision and biologically guided and technology-assisted orthopedic care. Advancements in diagnostic imaging, AI, minimally invasive surgery, robotic assistance, regenerative medicine, and tissue engineering have led to better diagnosis, precision in surgical procedure, and treatment options for patients with complex musculoskeletal conditions. At the same time, multidisciplinary rehabilitation, individualized pharmacologic treatments, and lifestyle modifications remain key aspects in maximizing functional rehabilitation and patient outcomes. While these positives are promising, there are still a number of issues to address, such as standardized treatment protocols, long term safety data, cost effectiveness data and larger scale clinical validation of emerging technologies. However, there is going to be need for future and efficient multicenter clinical trials, as well as the involvement of many other disciplines as well as advanced computational techniques in order to make regenerative and personalized medicine a reality. Taken together, all these could contribute to the formation of more personalized and efficient care pathways in orthopedics – which would go on to improve the quality of life in the future in the world.

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