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**The Role of Cognitive Strategies in Functional
Recovery During Rehabilitation Following Lower
Limb Fractures**

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“Sentirsi pieno di forza e di vigore, e il momento dopo pressoché impotente; essere in gran forma e in perfetta salute, e il momento dopo storpiato; godere del pieno possesso di tutte le proprie energie e facoltà, e il momento dopo esserne privo: è difficile comprendere un cambiamento così drastico e repentino, e la mente annaspa in cerca di spiegazioni.”

“To be full of strength and vigor one moment and virtually helpless the next, in the pink and pride of health one moment and a cripple the next, with all one’s powers and faculties one moment and without them the next—such a change, such suddenness, is difficult to comprehend and the mind casts about for explanations.”

Oliver Sacks, A Leg to Stand On

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Abstract

The management of lower limb fractures following surgery varies depending on when weight-bearing progression is prescribed. Prolonged immobilization and weight-bearing restrictions can delay recovery, as the absence of mechanical stimuli negatively impacts healing and motor control. Additionally, reduced movement is associated with decreased cortical activation, which may further hinder recovery.

Current rehabilitation protocols focus on reducing inflammation, managing pain and restoring joint mobility and strength. Less emphasis is placed on motor control alterations in patients without central nervous system injuries. Recent studies suggest that minimizing immobilization periods and allowing earlier weight-bearing improves recovery. Furthermore, cognitive strategies used in neurorehabilitation, such as motor imagery, have been shown to enhance motor performance and accelerate recovery in musculoskeletal injuries.

This doctoral research investigates the integration of cognitive strategies into rehabilitation protocols for lower limb fractures. Study 1 compares functional recovery and load management between two cohorts: one prescribed early weight-bearing and the other instructed to remain non-weight-bearing for 4 to 12 weeks. Study 2 evaluates the benefits of incorporating an antigravity treadmill with non-immersive virtual reality in patients undergoing surgical fixation for complex fractures, comparing it to traditional physiotherapy. Study 3 explores the use of motor imagery exercises in patients treated conservatively with casting and non-weight-bearing restrictions, assessing whether cognitive strategies can mitigate central motor control alterations after shorter immobilization periods.

Clinical data were collected using self-reported questionnaires, motion analysis and optokinetic gait analysis. Assessments were conducted at 6 weeks, 3 months and 6 months post-surgery to track the evolution of motor control recovery. The overall aim is to preserve

cortical activation, reduce the adverse effects of immobilization and enhance functional recovery, ultimately decreasing time away from work and healthcare costs.

Keywords: Fracture, Rehabilitation, Treadmill, Motor Imagery, Gait Analysis

Introduction

Immobilization following a lower limb fracture is a standard protocol aimed at ensuring proper healing and recovery. The process typically involves the use of casts, splints, or other immobilization devices designed to restrict movement and stabilize the fractured bone. While immobilization is crucial for bone repair, it can have significant implications beyond mere fracture healing. For example, it can lead to muscle atrophy, joint stiffness and decreased functional capacity, impacting patient's overall quality of life and recovery trajectory. Understanding these consequences is vital for optimizing patient outcomes and guiding rehabilitation strategies.

While immobilization is essential for fracture healing, its consequences on muscle mass and joint function underscore the importance of a comprehensive rehabilitation approach. Addressing these issues requires a multidisciplinary strategy that includes not only fracture management but also proactive measures to prevent the loss of function.

Traditionally, fractures have been addressed solely as musculoskeletal issues, without considering the broader implications that a post-traumatic fracture might have on other levels, including psychological and neuroplastic dimensions.

The literature reviewed in this thesis and the experiences documented over these years suggest an alternative approach to interpreting recovery after a lower limb fracture. This perspective not only addresses joint and muscle strength recovery but also incorporates the components of movement planning and the resultant motor actions, which are necessarily compromised due to the fracture and the subsequent period of restricted movement.

This thesis presents the doctoral project completed over the past three years, which monitored the recovery process following lower limb fractures in patients affiliated with the Orthopedic and Traumatology Clinical Operational Unit at the Cattinara Hospital in Trieste.

The thesis is structured into 4 chapters:

Chapter 1 introduces the issue of managing lower limb fractures, starting from the moment of hospitalization and extending to the final stages of functional recovery. The decision to stabilize a fracture either surgically or through immobilization in a cast or brace is always accompanied by instructions from the operating surgeon. These guidelines may vary, ranging from underload to a complete prohibition on weight-bearing.

Secondly chapter 1 reviews the existing literature on physiotherapeutic interventions aimed at overall recovery following lower limb fractures. The literature emphasizes the importance of early and tailored rehabilitation strategies to enhance functional outcomes. Studies indicate that comprehensive physiotherapy programs, which may include modalities such as strength training, balance exercises and proprioceptive training, significantly improve recovery times and functional mobility compared to traditional approaches that delay rehabilitation until after initial healing. Specific interventions, such as gait training and range-of-motion exercises, are highlighted for their roles in restoring movement and preventing complications associated with immobilization.

Chapter 2 delves into the neuroplastic phenomena that arise in response to limb immobilization, shedding light on the brain's ability to reorganize and adapt to the loss of mobility and sensory input. Prolonged immobilization, such as that seen after surgery or injury, often results in cortical reorganization, where regions of the brain responsible for motor control and proprioception undergo significant changes. This chapter reviews the current evidence

detailing these adaptive responses, emphasizing how immobilization can lead to altered neural circuits and functional representations in the motor cortex.

In addition Chapter 2 considers rehabilitation strategies that leverage the brain's capacity for reorganization. Emerging evidence supports the use of neuroplasticity-driven techniques such as motor imagery and action observation as powerful tools for rehabilitation. These techniques involve the mental rehearsal of movements (motor imagery) or the observation of others performing movements (action observation). They have been shown to activate similar neural pathways as actual physical movement. The integration of these methods into traditional rehabilitation programs may not only accelerate motor recovery but also improve functional outcomes by promoting brain-driven adaptation.

Chapter 3 introduces three experimental approaches, each comparing different rehabilitation strategies for the management of patients with lower limb fractures. Each study investigates a distinct approach to post-fracture care, ranging from early versus delayed weight-bearing, to the integration of advanced technologies such as antigravity treadmills with virtual reality and the application of cognitive strategies like motor imagery.

The overarching aim of this research is to evaluate the effects of physiotherapy combined with neuroplasticity-guided interventions in minimizing the adverse effects of immobilization following fracture and surgical intervention. Specifically, the studies seek to determine how various treatment strategies influence motor recovery by assessing both clinical and functional outcomes, despite the differences in patient populations presented.

A central focus is placed on the evaluation of motor control and functional integration of the injured limb during dynamic and static tasks. This is achieved through detailed motion analysis, including gait assessment and task-specific load management, to understand how the affected limb is reintegrated into whole-body movement during the recovery process.

The presentation of the contents follows a structured timeline as outlined: 1. to investigate differences in load management between patients allowed early weight-bearing and those required to adhere to a minimum of 6 weeks of weight-bearing restriction; 2. to present rehabilitation programs for patients who are not eligible for the *Early Weight Bearing procedure*, in order to observe the implications. By combining patient-reported outcomes with objective movement data, this thesis contributes to a better understanding of how different rehabilitation interventions may optimize recovery trajectories and support the development of more effective, individualized rehabilitation protocols for patients with lower limb fractures.

Chapter 4 presents the reflections drawn from the three years of research conducted, focusing on the potentialities and limitations of the various interventions explored, particularly in relation to the studies discussed. This chapter synthesizes the findings, provides insights into the effectiveness of different rehabilitation approaches and highlights areas for future research. The discussion encompasses not only the clinical implications of these findings but also the broader context of rehabilitation practices in managing lower limb fractures. Through this comprehensive analysis, the chapter aims to contribute to the ongoing discourse on optimizing recovery strategies and improving patient outcomes in this field.

Chapter 1: Lower Limb Complex Fractures

Fractures of the lower limbs contribute to substantial disability, necessitate prolonged treatment and recovery and constitute the majority of in-hospital surgical procedures (Fonseca et al., 2019; Wu, et al., 2019).

Fractures of the ankle and tibia account for 10.9 % of all fractures encountered by orthopedic surgeons in daily practice (Court-Brown & Caesar, 2006).

Ankle fractures represent a significant portion of musculoskeletal injuries in the adult population, ranking as one of the most frequently encountered types of fractures. The incidence of ankle fractures is estimated at around 137 cases per 100,000 individuals annually (Elsøe et al., 2018). This high incidence is particularly notable among two distinct groups: athletes, who are prone to such injuries due to high-impact and high-risk physical activities and elderly individuals, who often experience these fractures as a result of falls or decreased bone density associated with aging (Oladeji et al., 2020).

The prevalence of ankle fractures is distributed relatively equally between men and women (Elsøe et al., 2018).

The impact of ankle fractures extends beyond immediate injury, affecting long term functional outcomes and quality of life. Post-injury complications such as chronic pain, limited range of motion and instability can persist, particularly in cases involving complex fractures or inadequate management (McPhail et al., 2012). Rehabilitation and treatment strategies must address not only the acute management of the fracture but also prioritize the prevention of long-term functional impairment. This includes implementing tailored postoperative strategies that enhance both mechanical stability and the biological healing environment necessary for optimal recovery (De Vries et al., 2005).

Malleolar fractures are prevalent and are the third most common type of fracture in North America (Dehghan et al., 2016), with an estimated average incidence of 10.3 per 100,000 per year (Elsoe et al., 2015). These injuries typically result from rotational forces that cause twisting of the foot relative to the leg axis.

Various classification systems exist for malleolar fractures. Among them, the descriptive classification categorizes based on the number and location of affected malleoli: unimalleolar fractures (approximately 60-70% of cases) involve either the fibular or tibial malleolus; bimalleolar fractures (around 15-20% of cases) affect both the tibial and fibular malleoli; and trimalleolar fractures (about 7-12% of cases) also involve the posterior margin of the tibial plafond, often referred to as the "*third malleolus*" (Patel et al., 2023).

Intra-articular fractures of the proximal tibia, more commonly referred to as tibial plateau fractures. They represent about 1% of all fractures in the adult population affecting two main age groups among these patients: young male who sustain injuries after high energy trauma (road traffic accidents) and older female patients who sustain these injuries after low-energy trauma (simple falls) (Iliopoulos et al., 2020).

In the past decade, there has been a notable rise in the average age of patients (+7.4 years; $p = 0.10$), a 68% increase in incidence ($p < 0.05$) and a greater prevalence of low-energy trauma, particularly among elderly women (Bormann et al., 2023).

These types of fractures are particularly noteworthy due to their complex nature and the frequent requirement for both surgical intervention and extensive rehabilitation. They have a significant impact on the patients' lives and the health care system and the patients are not able to return to work for up to 4 months after surgical fixation (Kraus et al., 2018).

Despite the incidence of these fractures, they have received substantial attention in the literature (Court-Brown & Caesar, 2006), with numerous studies highlighting the considerable impact these fractures have on patient mobility and quality of life.

In recent years, clinical practice has shifted towards a more comprehensive evaluation of patients after fractures, which should not rely solely on x-ray indices (Belcher et al., 1997), but also considers physical functioning and activity levels. This includes assessing the relationship between clinical indicators such as range of motion, muscle strength and pain and the level of participation in daily and social activities (Van Son et al., 2016).

The combination of joint involvement and soft tissue injuries often complicates both the immediate management and long-term outcomes for these patients, emphasizing the need for comprehensive treatment strategies and targeted rehabilitation protocols.

Complex musculoskeletal injuries involving both joint and soft tissue damage present significant challenges in management and rehabilitation. Tibial plateau fractures, for instance, often involve multiple injured structures, requiring a comprehensive approach beyond just addressing the bone injury (Adams & Loeffler, 2020). Combined complex ligament injuries of the knee are particularly devastating, requiring specialized surgical and rehabilitation strategies (Romeyn et al., 2008).

In addition to the direct costs associated with ankle fractures, which a recent review estimated to range between \$1,908 and \$19,500 worldwide (Bielska et al., 2019), there are also significant 'indirect' costs, such as loss of productivity and informal care costs. These indirect costs contribute to nearly half of the total expense and carry even greater weight from a societal perspective (Noback et al., 2020; Baji et al. 2024).

These types of fractures affect individuals of all ages, with the majority being of working age. Beyond long-term disability and pain, the consequences of these fractures include time off work and various economic impacts (Dehghan et al., 2018)

Lower extremity fractures, including hip fractures, often result in persistent physical impairments, with effects such as deficits in range of motion and reduced muscle strength lasting for six months or longer (Hong et al., 2013; Van Son et al., 2016).

Traditional assessments of lower extremity fractures, relying mainly on X-ray imaging, often fail to capture the full extent of functional impairment. While physical impairment, such as reduced range of motion, decreased muscle strength and pain are correlated with disability, they account for only a small portion of the variance in long-term disability outcomes (Mock et al., 2000). Other factors, such as socioeconomic status, preinjury health and social support, also play important roles in determining long-term disability outcomes (Mock et al., 2000). Studies have found that patients experience moderate levels of dysfunction six months post-injury, with particularly high scores in ambulation, work and recreation (Mackenzie et al., 1993; Faergemann et al., 1998). To fully understand recovery, it is crucial to include patient-reported outcomes like health status (HS), health-related quality of life (HRQOL) and overall quality of life (QOL). HS typically reflects self-reported functional abilities, while QOL includes subjective evaluations of overall functioning and well-being. HRQOL specifically addresses the aspects of QOL affected by the disease. Despite their importance, these outcomes are not extensively studied in patients with extremity fractures (Van Son et al., 2016).

For example, an ankle fracture may hinder a patient's ability to climb stairs, impacting their HS. However, if the patient lives in a building with an elevator, this limitation might have less impact on their quality of life.

1.1 Lower limb complex fracture surgery

The typical management approach for tibial plateau fractures, similar to the other joint fractures, is surgical, most often performing open reduction and internal fixation (ORIF) (Canton et al., 2022) in acute settings. Exceptions include extensively open fractures, which are initially managed with external fixation as part of Damage Control Orthopedics (DCO) and non-displaced fractures. The objective of the surgery is to maintain the alignment of the bone fragments until complete bone healing occurs. For non-displaced cases, treatment may involve immobilization with a hinged knee brace or a long-leg cast for a duration of 4-6 weeks (Schatzkler et al, 1979; Ziran et al., 2007).

The primary goal of surgical intervention is to achieve accurate anatomical reduction and stable fixation, allowing for early mobilization to prevent post-traumatic knee stiffness. (Bonzanini et al., 2022). Surgical intervention may involve either open techniques or direct arthroscopic methods. When fragments are separated, they are reduced and stabilized using either individual screws or a combination of plates and screws. Ensuring sufficient stability in the final fixation is crucial to enable early mobilization of the knee and to prevent the development of joint stiffness (Prat-Fabregat et al., 2016).

Fracture management varies depending on the fracture type and location. Articular fractures often necessitate absolute stability through osteosynthesis, whereas diaphyseal fractures are typically addressed with intramedullary nailing, which provides relative stability and permits early weight-bearing (Norris et al., 2018). Intramedullary nails generally withstand higher mechanical stresses than plates; however, this advantage decreases in cases of unstable fractures (Charles-Harris et al., 2008). The decision between absolute and relative stability in minimally invasive plate osteosynthesis for simple distal metaphyseal or diaphyseal tibia fractures plays a significant role in healing outcomes. A comparative study between lag screw and neutralization plate (LSN) and bridge plate techniques revealed that the LSN group

achieved radiological union more quickly (19 weeks vs. 27 weeks), without a rise in complication rates (Wenger et al., 2017). Thus, understanding the biomechanical environment and the stability provided by surgical devices is crucial for optimizing fracture healing and ensuring successful patient recovery (Norris et al., 2018).

According to the AO Surgery Reference guidelines (AO Foundation Surgery Reference, 2024), the management of tibial plateau fractures involves strict non-weight bearing for a minimum of 10–12 weeks. The primary goal during the early postoperative phase is to achieve as full a range of motion as possible within the first 4–6 weeks through passive and active mobilization. In the absence of other injuries or complications, mobilization may begin as early as postoperative day 1, with particular emphasis on active knee and ankle movements.

Malleolar fractures range from isolated distal fibular fractures with minimal displacement to trimalleolar fractures with dislocation and potential vascular compromise. In these cases, achieving anatomical reduction and ensuring absolute stability is essential to facilitate early joint rehabilitation. (Gougoulis et al., 2010).

For bi- or trimalleolar fractures, in cases where stable fixation has been achieved, AO Surgery References guideline (AO Foundation Surgery Reference, 2024) recommend early active exercises and light partial weight-bearing starting from the first postoperative day. Weight-bearing should be progressively increased as tolerated by the patient. In fractures requiring reduction, the plaster cast should not be removed before 9–12 weeks or until the patient can walk pain-free in the cast. The duration of cast immobilization can be shortened based on the surgeon's discretion. After cast removal, rehabilitation should focus on intensive ankle and foot mobilization over an extended period. Weight-bearing is permitted in stable fractures, with cast removal typically occurring after 6–8 weeks, followed by 2–4 weeks of physiotherapy.

When managing lower limb fractures that require surgical intervention, orthopedic surgeons are often faced with the decision of implementing either an early weight-bearing protocol or a more conservative, restrictive approach to postoperative care (Meys et al., 2019; Kalmet et al., 2022). The choice of postoperative management strategy is critical and should be tailored to the type of fracture, the method of fixation and the patient's overall health status. Common surgical interventions include internal fixation with plates, screws, or intramedullary nails and in some cases, external fixation may be employed, particularly in complex or comminuted fractures.

The collaboration between orthopedic and plastic surgery is essential for the effective management of complex injuries, as it ensures optimal recovery of both bone and soft tissue structures (Mostafa et al., 2021). The diversity in fracture patterns, combined with patient-specific variables, highlights the importance of developing personalized postoperative strategies. Tailoring treatment plans to these factors is critical for achieving favorable long-term outcomes (Meys et al., 2019).

1.2 Lower limb complex fracture post-surgery management

Managing complications that arise from immobilization after surgical fixation of lower limb fractures presents significant challenges. Complications can delay the rehabilitation process and impede the restoration of normal function (Loubignac et al., 2022). Postoperative management must strike a delicate balance between early and restricted weight-bearing, each with distinct risks and benefits (Meys et al., 2019).

Postoperative loading presents a distinct advantage over immobilization by promoting early mobilization, which induces micromovements between adjacent bone fragments. These micromovements stimulate osteoblast activity, enhancing bone turnover metabolism, thereby facilitating fracture consolidation and promoting bone growth. (Goodship and Kenwright, 1985). Animal osteotomy models have demonstrated that moderate or controlled axial loading of the osteotomy site tends to enhance callus volume and reduce the time to union, compared to both the absence of loading and excessive early loading (Haller et al., 2013).

Early weight-bearing in patients promotes fracture healing by stimulating osteogenesis and maintaining joint function, potentially accelerating recovery and the return to daily activities (Kubiak et al., 2013). However, this approach carries risks, such as the possibility of losing fracture reduction, fragment migration, malunion, or nonunion if the bone has not sufficiently stabilized (Meys et al., 2019).

Conversely, a conservative approach involving prolonged immobilization and avoidance of weight-bearing can prevent mechanical stress on the healing fracture, reducing complications. The downside of this strategy includes muscle atrophy, joint stiffness and decreased mobility and muscle strength (Marusic et al., 2021). Prolonged inactivity can also exacerbate edema and lengthen rehabilitation, compromising long-term functional outcomes (Meys et al., 2019).

Thus, determining the optimal postoperative strategy - whether early weight-bearing or extended immobilization - should be individualized, considering factors such as fracture type, fixation method and the patient's overall condition and rehabilitation goals (Hoyt et al., 2012).

Recent research has begun to challenge the traditional paradigm of weight-bearing in fractures treated with plates and screws. Historically, articular fractures have been managed with an emphasis on achieving absolute stability (Hahn, 2004). However, recent findings indicate that early weight-bearing may not necessarily compromise outcomes. For example, a study by Williamson et al. (Williamson et al., 2018) found no significant loss of reduction or articular collapse in tibial plateau fractures that were allowed immediate full weight-bearing. Similarly, Striano et al. (Striano et al., 2022) reported no increase in complications in patients with distal femur fractures who began early weight-bearing. These insights reflect a shift in the understanding of fracture biomechanics, highlighting the importance of providing appropriate stability rather than strict adherence to absolute rigidity (Norris et al., 2018). Although early weight-bearing may offer physiological and socioeconomic advantages, it still requires careful consideration based on factors such as injury severity and bone quality (Williamson et al., 2018; Hahn, 2004).

A survey of Dutch surgeons revealed that 72.1% recommended earlier weight-bearing for tibial plateau fractures, with 55.9% initiating weight-bearing at six weeks (van der Vusse et al., 2017). Canton et al. (Canton et al., 2022) conducted a systematic review, concluding that early weight-bearing can be safe and effective in selected tibial plateau fracture cases. A retrospective study found no significant differences in outcomes between early and traditional weight-bearing protocols (Heiman et al., 2023). However, a scoping review indicated that non-weight bearing for 4-6 weeks remains common, with full weight-bearing typically recommended between 9-12 weeks, especially for more complex fractures (Arnold et al., 2017). Earlier studies also highlighted the risk of knee stiffness with as little as two weeks of

immobilization, further emphasizing the importance of early mobilization (Gausewitz & Hohl, 1986). Overall, there is a shift towards earlier mobilization and weight-bearing, though practices vary widely.

Technological advancements in orthopedic fixation techniques (Liang et al., 2024), combined with progress in physical rehabilitation, have transformed the treatment of lower limb fractures (Iliopoulos et al., 2020). These innovations have improved the precision of fracture fixation and rehabilitation outcomes, enabling faster and more effective recoveries (Iliopoulos et al., 2020). Despite these advances, the primary goal remains clinical improvement, focusing on preserving musculoskeletal integrity and minimizing complications like malunion, nonunion, or joint stiffness (Fonseca et al., 2019).

The duration and extent of weight-bearing restrictions depend on several factors, including fracture type, fixation quality, bone health and comorbidities that could affect healing (Gahr et al., 2023; Kalmet et al., 2018). Complex fractures, such as those involving the tibial plateau or acetabulum, often require longer non-weight-bearing periods to ensure precise anatomical restoration and prevent post-traumatic arthritis. Generally, patients are advised to avoid full weight-bearing for 6-12 weeks postoperatively, with weight on the affected limb limited to 20 kg to prevent excessive stress on the fracture and fixation construct (Vasarhelyi et al., 2006; Meys et al., 2019). During this period, regular clinical and radiographic assessments are essential to monitor healing progression (Gahr et al., 2023).

During the post-surgical rehabilitation phase, the focus is primarily on preserving the range of motion in adjacent joints, preventing muscle atrophy and managing pain and swelling (Hoyt et al., 2015). Physiotherapy is essential at this stage, incorporating techniques such as passive and active range of motion exercises, isometric strengthening and edema management to prepare the limb for eventual weight-bearing.

As bone healing progresses, supported by radiographic evidence of sufficient consolidation, a gradual introduction of weight-bearing is carefully initiated (Meys et al., 2019). This progression is closely monitored to prevent overloading the healing structures, with incremental increases in weight guided by the patient's pain tolerance, clinical evaluation and imaging results. A permissive weight-bearing protocol has shown potential benefits for patients with surgically treated fractures of the pelvis and lower extremities, with a median time to full weight-bearing of 12 weeks (Meys et al., 2019). However, studies indicate that only 32.3% of non-hip fracture patients are permitted immediate full weight-bearing following surgery (Richardson et al., 2022).

Additional studies provide evidence supporting the benefits of early weight-bearing in fracture rehabilitation. For instance, Stinner et al. (Stinner et al., 2022) demonstrated in a randomized trial that antigravity treadmill therapy, when compared to standard care for periarticular fractures, allowed safe limb loading and improved recovery. Similarly, Heiman et al. (Heiman et al., 2023) found no significant outcome differences between early (<10 weeks) and traditional (≥ 10 weeks) weight-bearing protocols for tibial plateau fractures. In a retrospective analysis, Williamson et al. (Williamson et al., 2018) reported that immediate full weight-bearing following plate fixation of tibial plateau fractures did not compromise fracture fixation or result in articular collapse within three months post-operation. These studies underscore the potential advantages of earlier weight-bearing, such as accelerated recovery and a reduction in complications associated with prolonged immobilization. However, despite these promising findings, clinical guidelines remain cautious, with recommendations often advising against weight-bearing for 6-8 weeks and delaying full weight-bearing until 12 weeks or complete fracture union for optimal healing and outcomes (Vasanad et al., 2013).

Partial weight-bearing is a component of postoperative management during the rehabilitation phase, in accordance with modern stable fixation concepts. Weight-bearing

typically begins on the first postoperative day and is progressively increased until full weight-bearing is achieved (AO Foundation Surgery Reference, 2024), but early weight-bearing is interpreted in some studies as beginning on the first postoperative day, while in others, it is initiated 1–2 weeks after surgery (Vasarhelyi et al., 2006).

The ultimate objective is to restore full functional mobility while minimizing the risk of long-term complications, such as chronic pain, joint stiffness, or post-traumatic osteoarthritis (Hoyt et al., 2015).

In conclusion, the post-surgical management of complex lower limb fractures requires a careful balance between protecting the fracture site and encouraging early mobility and functional recovery.

1.3 Consideration for the rehabilitation after lower limb fractures

A notable finding from the literature is the limited involvement of physical therapists and rehabilitation professionals in the planning, execution and publication of research on this clinical topic. Greater participation could enhance their understanding of the role they play in applying optimally dosed mechanical stimuli to improve recovery without causing harm. Physical therapists already have a theoretical foundation for guiding functional recovery after lower extremity fractures, based on tissue healing principles and basic science. However, clinical research in this area is still in its early stages, with limited low-level evidence. More investment and active involvement from the rehabilitation field are needed. Therapists should collaborate closely with referring surgeons to ensure safe, progressive weight-bearing, while acknowledging the current lack of strong evidence supporting this practice in all clinical scenarios (Flowers et al., 2022).

Given the significant impact that lower limb fractures have on patients' lives (Fonseca et al., 2019), clear guidelines on how to structure rehabilitation programs are essential. These guidelines would help reduce recovery time and minimize the period of inactivity, allowing patients to return to their normal daily activities more quickly.

Additionally, guidelines regarding weight-bearing (whether full or partial) are often quantified as a percentage of the patient's body weight or described in more general terms such as "non-weight-bearing," "partial weight-bearing," or "full weight-bearing." However, these general directives often do not provide physical therapists with clear instructions regarding the actual weight that the patient can safely apply to the operated limb. (Meys et al., 2019).

Furthermore, a study (Lajevardi-Khosh et al., 2019) reveals that patients often report difficulties in adhering to weight-bearing restrictions when prescribed a non-weight-bearing status, or they may not comply at all. Providing clearer explanations on how to manage load during daily activities, including the use of assistive devices such as Canadian crutches or a

cane, could facilitate recovery for those patients who tend to avoid using the operated limb. This approach would also support those who struggle to adhere to weight-bearing restrictions, ultimately promoting a more effective management of their rehabilitation process.

Establishing a clear guideline for postoperative rehabilitation while avoiding excessive loads on the bony structure is quite complex due to individual patient characteristics, the amount of mineral bone content and the type of instability created by the specific fracture. These factors can significantly alter postoperative recommendations, making it essential to tailor rehabilitation protocols to each patient's unique circumstances to ensure optimal recovery outcomes. Proper rehabilitation can improve clinical outcomes and shorten hospital stays (Lee et al., 2020). However, protocols vary widely, highlighting the need for further research to determine optimal rehabilitation strategies for different fracture types and patient populations (Arnold et al., 2017; Lee et al., 2020).

Meys et al. (Meys et al., 2019) proposed a protocol that defines the estimated timeframe for achieving treatment goals and the appropriate weight-bearing intensity by comparing predictive factors, patient profiles and treatment objectives with surgical outcomes. This approach allows for a more tailored rehabilitation strategy, ensuring that weight-bearing recommendations are aligned with the individual needs and recovery trajectories of patients following lower limb fractures.

A structured approach that contrasts with traditional methods by allowing for more flexible weight-bearing guidelines tailored to individual patient profiles, has led to a significant improvement in recovery times, with 50% of patients achieving full weight-bearing within 12 weeks, approximately 4 weeks earlier than those managed according to AO guidelines (AO Foundation Surgery Reference, 2024). This reduction in recovery time underscores the

protocol's effectiveness in enhancing rehabilitation outcomes and minimizing the duration of limited mobility (Meys et al., 2019).

1.4 Lower extremities: a comprehensive approach

The rehabilitation of lower limb fractures necessitates a comprehensive understanding of the specific roles of the joints involved. These joints are vital for facilitating complex movements, ensuring stability and supporting the mechanical functions required for both locomotion and weight-bearing.

The ankle joint is a complex and dynamic structure that plays a pivotal role in human locomotion (Brocket and Chapman, 2016). Its functions are integral to maintaining balance, absorbing shock and facilitating forward propulsion during walking and running (Lee et al., 2016).

During the initial contact phase of gait, when the heel strikes the ground, the ankle performs a critical function in shock absorption. The subtalar joint, part of the ankle complex, allows for controlled pronation, which helps dissipate the forces transmitted through the limb upon ground contact (Hargrave et al., 2003). The tibialis anterior muscle, which dorsiflexes the foot, controls the rate at which the foot lowers to the ground, thereby moderating the impact force (Maharaj et al., 2019).

As the body moves into the midstance phase of gait, the ankle joint provides stabilization, ensuring that the body's weight is effectively supported on one leg (Winter, 1980).

One of the most critical functions of the ankle is its role in propulsion during the terminal stance and pre-swing phases of gait (Lee et al., 2016). As the body moves over the foot and prepares for toe-off, the ankle plantarflexes, driven by the powerful contraction of the gastrocnemius and soleus muscles (Brocket and Chapman, 2016). This plantarflexion generates the necessary force to propel the body forward, effectively initiating the swing phase of the gait cycle (Neptune et al., 2001).

The efficiency of this propulsion is vital for achieving a smooth and energy-efficient gait. Impairments in ankle function, such as weakness in the plantarflexors or limited range of motion, can lead to reduced propulsion, resulting in a shorter stride length and increased energy expenditure during walking (Huang et al., 2015).

During the swing phase of gait, the ankle must dorsiflex to ensure that the toes clear the ground as the limb advances (Bajelan et al., 2024). Additionally, the ankle prepares for the next stance phase by positioning the foot for optimal ground contact (Chinn et al., 2011).

Proper foot clearance is essential for maintaining an efficient and safe gait pattern. Conditions that affect the ankle's ability to dorsiflex can significantly impair mobility and increase the risk of falls (Nagano et al., 2022).

The ankle joint also plays a key role in adapting to uneven terrain. The flexibility of the ankle allows for adjustments in foot positioning to maintain stability when walking on slopes, stairs, or irregular surfaces (Morris, 1997).

The knee plays a crucial role in maintaining stance stability, as its function directly impacts the entire lower limb during both the stance and swing phases of gait. Proper knee alignment and control ensure balance and load distribution throughout the limb, stabilizing the body during weight-bearing activities (Winter, 1980). Additionally, knee flexion and extension influence foot clearance and positioning during the swing phase, contributing to efficient movement and reducing the risk of injury or instability (Kent et al., 2021). Without optimal knee function, both stance and swing phases can be compromised, affecting overall gait mechanics.

The knee joint fulfills four key functional obligations that ensure efficient and stable locomotion (Perry & Burnfield, 2010). When the foot makes contact with the ground, the knee joint flexes slightly to absorb the impact forces transmitted through the limb (Derrick, 2004).

This flexion is critical as it helps to reduce the vertical forces that would otherwise be transmitted directly to the hip and lower back, potentially leading to injury.

In addition to shock absorption, the knee must provide extensor stability during the stance phase to ensure secure weight bearing. As the body moves over the supporting limb, the knee must remain stable to support the body's weight without collapsing into excessive flexion (Winter, 1980).

Extensor stability is particularly important in the early stance phase, known as the loading response, where the knee experiences significant forces as the body's center of mass shifts forward (Munsch et al., 2023).

During the swing phase of the gait cycle, the knee must rapidly flex to allow the foot to clear the ground. This movement is essential for preventing the foot from dragging, which could cause tripping or stumbling. Typically, the knee flexes to approximately 60-70 degrees during the initial swing (Paterno et al., 2008).

The final obligation of the knee during walking occurs towards the end of the swing phase when the knee must extend to prepare the limb for the next stance phase. This extension is critical for ensuring that the foot lands correctly on the ground, facilitating a smooth transition into the next gait cycle (Tanaka et al., 2021).

All these functions are critically dependent on activity and could be markedly impaired during periods of immobilization following a fracture.

The joints of the human body serve not only biomechanical functions such as support and movement but also house a complex sensory system. This system provides essential information to the central nervous system (CNS) for motor control and coordination (Riemann and Lephart, 2002). Composed primarily of mechanoreceptors and sensory afferents, this

sensory system enables precise perception of joint position, movement and load functions crucial for maintaining balance and executing complex motor activities (Dean, 2013).

Proprioceptive signals are transmitted throughout the CNS and are vital for efficient motor control and sensorimotor regulation of dynamic stabilizers. The informative functionality of joint structures refers to their ability to continuously send data to the CNS, allowing the body to anticipate and adapt to environmental changes and functional demands. This adaptability occurs primarily through feedforward mechanisms (Chiel et al., 2009).

Proprioception is essential for regulating the activation of dynamic restraints and motor function. Increased muscle stiffness, largely mediated by muscle spindles, is believed to be a key factor in maintaining joint stability. Articular mechanoreceptors influence gamma motor neuron activity, which in turn affects muscle stiffness. Furthermore, these mechanoreceptors contribute to higher-level motor control of dynamic restraints, enabling the body to anticipate and respond efficiently to movement demands. This coordination ensures smooth and effective motion (Riemann and Lephart, 2002; Sousa et al., 2012).

An illustration of this concept can be observed in the knee joint, where ligaments are equipped with various mechanoreceptors, such as Ruffini endings, Pacinian corpuscles, Golgi tendon organs and free nerve endings. These receptors play a crucial role in relaying vital information to the central nervous system (CNS) about joint position, movement and potentially harmful stimuli. While low-threshold mechanoreceptors in the ligaments have minimal and infrequent effects on alpha-motoneurons (skeletal motor neurons), the influence on the surrounding tau-muscle spindle system is profound. Even slight stretching of the ligaments can lead to significant alterations in the responses of muscle spindle afferents. Since these primary muscle spindle afferents are essential for modulating muscle stiffness, the mechanoreceptors in the knee ligaments are likely involved in the preparatory adjustment of

muscle stiffness around the joint. This process is crucial for maintaining joint stiffness and ensuring overall functional stability (Johansson et al., 1991).

Immobilization, such as after a fracture, could significantly compromise the mechanical and sensory functions of the ankle and knee. Immobilization disrupts the proprioceptive feedback loops that are vital for the CNS to predict and adapt to the physical demands placed on the body (Roll et al., 2012; Moisello et al., 2008). This disruption can delay recovery, as the body's ability to prepare for and adapt to movement is hindered, increasing the risk of further injury during rehabilitation. Prolonged immobilization can lead to a decrease in proprioceptive acuity, which further impairs motor control and balance during the post-immobilization phase (Caplan et al., 2015). Moreover, the loss of proprioceptive input can lead to altered neuromuscular control, resulting in a greater reliance on visual (Moisello et al. 2008) and vestibular inputs or in different response strategies (Horlings et al. 2009), for balance and coordination.

The implications of the above are particularly important in rehabilitation, where a gradual reintroduction of weight-bearing and movement is essential to restore both the functional and sensory capacities of the affected joints (Hoyt et al., 2015). Addressing sensory and proprioceptive deficits resulting from injuries is therefore a critical aspect of successful post-fracture rehabilitation strategies (Lephart et al., 1997). Understanding these impairments and incorporating proprioceptive training into recovery programs can significantly enhance motor control, joint stability and overall functional outcomes.

Considering the specific characteristics of the lower limb discussed thus far, it is possible to acknowledge that even in the absence of weight-bearing, other functions of the lower limb can be trained and preserved from both motor and sensory perspectives. The

proposal for early rehabilitation programs during the initial phase of immobilization or postoperative recovery, focused on maintaining perceptual processes, body awareness and spatial orientation of the limb, as previously suggested in neurorehabilitation (Lee et al., 2015), may effectively prepare the lower limb structures for subsequent weight-bearing rehabilitation. This proactive approach could potentially mitigate the risk of extending recovery times.

1.5 Physiotherapy after lower limb complex fractures

The rehabilitation of lower extremity injuries encompasses a multi-phase approach, tailored to the specific needs of patients from the acute phase through to long-term recovery. Initially, in the acute phase, the primary focus is on alleviating pain, reducing swelling and protecting the injured (Bodrova et al., 2023). During the rehabilitation phase, the goal is to significantly improve muscle strength, endurance and overall functional mobility, with specific attention to preparing the patient for a return to daily activities or sports (Hoyt et al., 2015). Advanced rehabilitation programs progress from simple activities to complex, specific movements, incorporating strength, flexibility, agility and proprioceptive training (Lephart & Henry, 1995).

The approach currently employed by musculoskeletal physiotherapists in selecting exercises and rehabilitation strategies is primarily guided by exercise protocols validated in clinical trials, as well as general guidelines and recommendations provided by orthopedic surgeons. (Snodgrass et al., 2014;)

The existing literature contains limited information on the rehabilitation of patients with tibial plateau fractures. Most research concentrates on the types of fixation methods used or the clinical outcomes following fixation (Iliopoulos, 2020). Consequently, there is a notable scarcity of comprehensive and consistent information regarding the rehabilitation protocols for patients undergoing surgical fixation for tibial plateau fractures. When such information is available, it is often fragmented and varies significantly across studies.

In a 2020 systematic review (Iliopoulos et al., 2020), the authors aimed to identify guidelines concerning exercises for range of motion recovery, immobilization and weight bearing following tibial plateau fractures. In this review, the authors conclude that the literature on this topic is limited and controversial.

Early mobilization exercises for the joint should be encouraged as soon as possible post-surgery. Immobilization following plate fixation does not appear to offer significant benefits (Iliopoulos et al., 2020) and the decision regarding weight-bearing is highly debated (Van der Vusse et al., 2017). Recent trends suggest that early weight-bearing is preferred by many experts as a post-surgical guideline. Balancing early recovery with proper fracture stabilization is crucial to optimize the range of motion for each patient (Iliopoulos et al., 2020).

From the results of the systematic review, Iliopoulos and his colleagues (Iliopoulos et al., 2020) concluded that rehabilitation timing can vary based on the surgical technique. For external fixator bridge stabilizations where knee movement is restricted, exercise initiation is delayed until after the fixator removal and subsequent definitive surgery. In contrast, circular or articulated external fixators allow immediate mobilization. When the knee is not constrained by the fixator, exercises should be encouraged as early as possible. Immobilization with an articulated brace is used post-internal fixation, but its benefits are inconsistently reported, with some studies indicating worse functional outcomes for patients immobilized beyond six weeks (Polat et al., 2019). Therefore, immobilization for more than two weeks post-surgery is generally not recommended.

Post-operative rehabilitation strategies for ankle fractures exhibit considerable variability and often lack standardized definitions. This inconsistency poses significant challenges in evaluating the effectiveness of various rehabilitation protocols. Post-operative rehabilitation is considered a key area of ankle fracture care research, primarily focusing on comparing, manual therapy (Lin et al., 2008), exercise therapies (Altuwairqi, 2024) or device-based (Tang and Xiao, 2020) therapies, as well as weight-bearing strategies (Sharma and Farrugia, 2022). Early initiation of active ankle exercises and weight-bearing seems to be

linked to a faster return to work and daily activities compared to prolonged immobilization (Smeeing et al., 2015). However, a challenge remains in encouraging patients to consistently continue physiotherapy at home, promoting self-management through ankle exercises and adherence to physiotherapy protocols, where barriers such as anxiety, stress and low self-efficacy can impede adherence (Bretherton et al., 2024).

Other studies have been conducted to identify the optimal rehabilitation strategy, combining physical therapies with exercise programs. However, no significant improvement was observed with the use of any additional therapy compared to exercise alone. (Moseley et al., 2015).

Considering that the cost of physiotherapy for complex fractures is substantial, averaging £546.27 per case of tibial fractures in the UK (Barron et al., 2013), it underscores the necessity for realistic costing plans within healthcare systems. This financial burden emphasizes the importance of efficient resource allocation and planning in order to provide adequate rehabilitation services.

Moreover, existing evidence indicates that effectively addressing patients' physiotherapy needs following lower-extremity trauma is associated with improved outcomes across various dimensions, including physical impairment and functional limitations (Castillo et al., 2008). Meeting these needs not only enhances recovery but also contributes to long-term well-being and quality of life for patients.

Chapter 2: Central Nervous System Reorganization as a Consequence of Immobilization

Despite advancements in technology and surgical techniques designed to expedite recovery times after fractures, it is essential to recognize that the commonly prescribed treatment for these patients tends to focus primarily on the healing of the fractured site itself. However, this approach often overlooks the alterations that may occur at the central nervous system level following an injury (Snodgrass et al., 2014).

Such central effects can significantly interfere with the overall recovery process, particularly when patients attempt to return to their daily activities after extended periods of non-weight bearing, restricted movement, or immobilization in a cast. While physiotherapists addressing musculoskeletal dysfunction typically concentrate on region-specific movement and exercises (Snodgrass et al., 2014), it is vital to expand the scope of rehabilitation to include considerations of the central nervous system's role in recovery. By acknowledging and addressing these central alterations, rehabilitation programs can be more comprehensive and ultimately lead to better outcomes for patients as they reintegrate into their normal routines.

Following lower limb surgery, patients may experience postural instability due to secondary dysfunction such as muscle weakness (Caplan et al., 2015) and reduced proprioception from immobilization (Hall et al., 2016). A study found that short-term cast immobilization of a unilateral lower extremity along with physical inactivity induced postural instability during standing in healthy young men (Ikeda et al., 2023).

There is evidence that the central nervous system undergoes changes in response to musculoskeletal dysfunctions (Moseley and Flor, 2012). This phenomenon, known as neuroplasticity, refers to the central nervous system's intrinsic ability to undergo continuous

changes and reorganize itself by forming new neural connections, which can be both adaptive and maladaptive, in response to alterations in its afferent inputs and efferent targets. These changes are constantly triggered by previous events or result from intrinsic remodeling activity (Pascual-Leone et al., 2005, Snodgrass et al., 2014).

Neuroplasticity encompasses several mechanisms, including synaptic plasticity, structural plasticity and functional plasticity. Synaptic plasticity involves changes in the strength of connections between neurons (Kondo, 2016), while structural plasticity refers to alterations in the physical structure of the brain, such as changes in dendritic spines and cortical maps (Li et al., 2021). Functional plasticity includes the reorganization of brain areas to compensate for lost functions or to enhance existing capabilities (Herdener et al., 2010).

Structural plasticity, often referred to as Hebbian plasticity, is a mechanism where simultaneous co-activation of neurons reinforces their synaptic connections (Li et al., 2021).

Experience-dependent plasticity is fundamental for learning new skills and adapting to environmental changes, as it describes how the brain reorganizes in response to learning and experience. Understanding this process has significant implications for neurorehabilitation (Martin et al., 2022; Hensch, 2005), but also in the absence of direct nervous system damage (Langer et al., 2012). The immobilization due to musculoskeletal injuries, such as fractures, may result in altered motor control and sensorimotor integration, with a decrease in cortical thickness in the primary motor and somatosensory areas (Langer et al., 2012).

Significant cortical reorganization, similar to that observed in central nervous system injuries and chronic pain, can also arise from disuse and altered sensory input in the musculoskeletal system. The disruption of the action-perception loop caused by limb immobilization prevents the brain from receiving kinesthetic feedback that typically arises from movement (Roll et al., 2012). The reduction of sensory afferent signals has been shown to be associated with anatomical and functional reorganization of the somatosensory cortex

following spinal cord injury, leading to maladaptive brain reorganization. (Vastano et al., 2022).

Neuroplasticity has been extensively recognized and demonstrated in the context of *chronic* musculoskeletal disorders (Pelletier et al., 2015). The experience of pain significantly activates and is generated by a broad network of cortical regions, collectively known as the "pain matrix," which includes the primary and secondary somatosensory cortices, insula, anterior cingulate cortex, amygdala, prefrontal cortex and thalamus (Reddan et al., 2018).

The "pain matrix" can be activated by touch, cognitive demand and even in the absence of nociceptive input (Legrain et al., 2011); for example, phantom limb pain continues to be felt long after an amputation (Ehde et al., 2000; Reddan et al., 2018). These experiences suggest that it is impossible to consider a peripheral alteration, such as a musculoskeletal injury, without acknowledging its impact on the central nervous system, which adapts itself in an experience-dependent modality.

Moreover, brain activation patterns vary depending on the location and nature of the pain experienced. For example, functional magnetic resonance imaging (fMRI) studies have shown increased activity in the medial prefrontal cortex among individuals with chronic low back pain, while patients with knee osteoarthritis exhibit heightened activation in the insular region (Apkarian et al., 2009)

Studies on Complex Regional Pain Syndrome (CRPS) further illustrate the phenomenon of maladaptive plasticity after musculoskeletal disorder. CRPS, particularly Type I, is a complex neurological disorder characterized by pain disproportionate to the injury, autonomic dysfunction and trophic changes (Dutton & Rhee, 2021). It can develop after trauma to an extremity with no or little nerve damage (Gofita et al., 2019) but can also occur

after conditions that necessitate limb immobilization and may significantly prolong the recovery time from the fracture itself (Dutton and Rhee, 2021).

The condition involves a complex interplay of symptoms such as spontaneous pain, hyperalgesia, allodynia, abnormal blood flow and sweating regulation, skin and subcutaneous tissue edema and trophic changes affecting the skin and its appendages (Baron, 2004). Additionally, CRPS is associated with both active and passive movement disorders (Van Hilten, 2010). These disturbances may be limited to a single extremity, typically remaining confined to its distal part (Jänig and Baron, 2002).

Multiple levels of neural integration are likely involved in CRPS, including the spinal cord, brainstem, diencephalon (hypothalamus, thalamus) and forebrain (cortex and limbic system) (Linnman et al., 2013). The clinical signs and symptoms in CRPS I are often disproportionate to the initial traumatic event (Harden et al., 2022), with the syndrome frequently persisting even after local changes from the trauma have healed (Bruehl, 2019). CRPS patients exhibit alterations in somatosensory systems that process noxious, tactile and thermal information, as well as in the sympathetic systems innervating the skin (blood vessels, sweat glands) and the somatomotor system (Jaenig and Baron, 2002). These changes suggest that the central representations of these systems are altered, which is reflected in the modified outputs of these systems.

The central changes, particularly in the thalamus and cortex, may be detectable through advanced imaging techniques such as functional MRI (fMRI) or positron emission tomography (PET) (Jaenig and Baron, 2022). Chronic CRPS I patients frequently exhibit generalized sensory deficits, potentially indicating irreversible changes in the brain induced by trauma also without nerve injury (Jaenig and Baron, 2022). These deficits may also correlate with neglect-like phenomena and disuse syndrome following immobilization (Punt et al., 2013).

It has been observed that the abolishment of afferent sensation from a limb lead to a form of learning based on the conditioned suppression of movement. This decreases the use of the limb in spontaneous movement (Taub et al., 2006; Taub et al., 1999).

The concept of "*learned nonuse*" was introduced to describe neuroplastic changes in the nervous system, with the brain deprioritizing the use of an affected limb following injury, pain, or immobilization (Taub et al., 2006). This alteration may decrease the cortical representation of the affected limb due to its reduced use and may result in muscle atrophy, reduced range of motion and delays in the rehabilitation process (Taub et al., 2006; Calford & Tweedale, 1991 – published in 2009).

From a functional perspective, immobilization after a fracture can lead to altered movement patterns that are learned before spontaneous functional recovery, a phenomenon referred to as "*learned misuse*" rather than "*learned nonuse*" (Taub et al., 1999).

Learned nonuse is particularly prevalent among patients recovering from neurological conditions, where individuals develop a habit of avoiding the use of an injured limb even after physical healing has occurred. This avoidance is often reinforced by the pain, discomfort, or difficulty experienced during the early stages of recovery, creating a vicious cycle that further diminishes the limb's functional capacity (Taub et al., 2006; Liepert et al., 2000).

Other studies had demonstrated that limb nonuse (or disuse) induces a reduction in the size and excitability of the cortical representation of the immobilized limb, gradually leading to maladaptive plasticity changes and the appearance of motor alterations (Huber et al., 2006; Avanzino et al., 2011; Langer et al., 2012).

Immobilization induces reduction of the corticospinal excitability of the immobilized limb as early as 10 hours post-immobilization, increasing the duration of the evaluated movement (Bassolino et al., 2012; Bassolino et al., 2014).

These changes facilitate the emergence and consolidation of compensatory behaviours, limiting the recovery of motor performance (De Marco et al., 2021).

Interestingly, studies on the short-term consequences of immobilization (Bassolino et al., 2012; Facchini et al., 2002) have been conducted on healthy volunteers, who do not experience the emotional impact that patients may face following a trauma that resulted in a fracture.

Prolonged immobilization, in addition to the systemic effects of a fracture, not limited to the local injury, can result in kinesiophobia (Kus et al., 2024). Fear of movement following lower limb trauma, often triggered by pain, may have long-lasting effects, persisting for up to two years after the injury (Archer et al., 2015). A recent study found that patients who underwent surgery, despite having more severe injuries and fractures, did not show greater kinesiophobia compared to those treated conservatively, provided both groups received similar physiotherapy treatment (Kus et al., 2024).

Recent studies highlight the significant impact of fear of movement and re-injury on fracture rehabilitation, showing that this fear can increase pain perception and delay functional recovery (Liu et al., 2021). Fear of movement, often intensified by the experience of a fracture, could lead to avoidance behaviors that worsen clinical outcomes and extend the rehabilitation period.

Recent studies have also demonstrated cortical functional changes following upper limb immobilization, both in healthy individuals subjected to immobilization (Moisello et al., 2008) and in patients with upper limb conditions requiring immobilization for at least two weeks

(Langer et al., 2012). As limb immobilization is a common intervention technique, it is crucial for therapists to recognize and understand both its beneficial and potentially detrimental effects (Langer et al., 2012).

2.1 Neuroplastic phenomena following limb immobilization: what we know from neuroimaging evidence

The neuroplastic changes induced by limb immobilization have been widely explored through experimental models of disuse and sensorimotor deprivation. These studies typically assess alterations in motor performance before and after immobilization, employing motor execution (ME) tasks (Huber et al., 2006) or transcranial magnetic stimulation (TMS) (Avanzino et al., 2011).

Consistent evidence suggests that immobilization results in decreased motor performance across various motor execution (ME) tasks. Huber et al. (Huber et al., 2006) demonstrated that immobilization negatively affects tasks requiring coordination and precision, such as pointing and reaching, allowing for the evaluation of performance changes before and after immobilization. This study indicates that immobilization leads to deterioration in motor performance, characterized by longer movement times and reduced accuracy, likely due to disruptions in joint coordination and increased variability in movement patterns (Huber et al., 2006).

Another recent study by MacLennan et al. (MacLennan et al., 2021) demonstrated that voluntary activation of the quadriceps femoris significantly declined after just 48 hours of knee joint immobilization in young females. The researchers assessed voluntary activation using electrical stimulation during maximal voluntary contractions.

Significant changes in motor performance are observed after 12 hours of immobilization, but not after 6 hours (Moisello et al., 2008). However, alterations in corticospinal excitability have been reported as early as 10 hours post-immobilization (Avanzino et al., 2011). Immobilization has been found to reduce motor-evoked potentials, indicating decreased excitability in the motor pathways associated with the immobilized limb.

Research shows that unilateral arm immobilization leads to notable changes in the motor cortex, including reduced cortical thickness and volume (Langer et al., 2012), reflecting neuroplastic adaptations due to disuse. Additionally, functional connectivity within the motor cortex shifts from unilateral activation to increased bilateral coactivation. This suggests a compensatory mechanism in response to the loss of input from the immobilized limb (Langer et al., 2012).

While overt motor impairments may require longer periods of immobilization to manifest, these findings indicate that neurophysiological changes in corticospinal pathways can occur relatively early, reflecting initial neural adaptations to reduced sensory and motor input (Avanzino et al., 2011). As previously discussed, the reduced activity in the primary motor cortex (M1) observed by Avanzino and colleagues was not solely due to the lack of voluntary movement but also linked to decreased proprioceptive feedback from the immobilized hand (Avanzino et al., 2011).

Other research has shown that corticospinal excitability can be significantly affected by limb immobilization in as little as 3 hours post-immobilization (Karita et al., 2017). Extended periods of immobilization have also been linked to both structural and functional changes within the brain (Burianova et al., 2016; Garbarini et al., 2019; Langer et al., 2012). In an earlier study, Liepert et al. (1995) used Transcranial Magnetic Stimulation (TMS) to detect notable differences in the cortical representation of an immobilized lower limb after 4 weeks of injury-related immobilization. These differences were compared to both the unaffected limb and a control group, with no significant changes seen after just 9 days of immobilization. However, reactivation of voluntary muscle use reversed these effects, indicating the alterations were temporary and primarily functional rather than permanent structural changes (Liepert et al., 1995).

In addition to TMS, Seo and colleagues (2004) incorporated EEG, MRI and functional connectivity analysis into their study, demonstrating that upper limb immobilization for 14 days in a group of young women resulted in strength loss without corresponding muscle atrophy (Seo et al., 2024). Their study further revealed alterations in brain resting-state functional connectivity following immobilization, particularly involving the supplementary motor area (SMA), ventral premotor cortex (vPMC) and cerebellum, which are implicated in neuroplastic changes due to muscle disuse (Gandola et al., 2019; Garbarini et al., 2019). Contrary to expectations, no changes in connectivity were observed in the primary motor (M1) or somatosensory (S1) cortices following immobilization (Seo et al., 2024). The enhanced functional connectivity between the bilateral supplementary motor area (SMA) and the immobilized cerebellar lobule VIIIa may suggest a compensatory process, in which the brain continues to plan movements normally performed by the immobilized arm. This is similar to the SMA's activation during interventions like motor imagery training (Jankelowitz & Colebatch, 2002), which mitigates strength decline by imagining movement without physical execution. After 14 days of upper arm immobilization, this enhanced connectivity likely reflects the brain's heightened effort to maintain previously learned motor commands (Seo et al., 2024).

The heterogeneity of results across studies may be attributed to differences in methodological choices by researchers. In some cases, the upper limb was immobilized (Avanzino et al., 2011; Seo et al., 2024), while in others the lower limb was immobilized (MacLennan et al., 2021). This difference plays a distinct role in motor function. Additionally, some studies focused on the dominant limb (Langer et al., 2012), whereas others examined the non-dominant limb (Seo et al., 2024). These variations in experimental design likely contribute to the differing outcomes observed.

The studies presented thus far have outlined how immobilization and disuse of a limb lead to consequences affecting the entire system. However, plastic changes, due to their inherent nature, are reversible through the reintroduction of movement. Furthermore, the "altered" system, to maintain its functional organization, can also adapt to the new condition by implementing strategies that prevent the establishment of these alterations.

In a study by Garbarini et al. (2019) utilizing transcranial magnetic stimulation (TMS), electromyography (EMG) and functional MRI (fMRI), it was observed that heightened activity in the right ventral premotor cortex (vPMC) occurred immediately following the immobilization of the left hand. However, after one week of immobilization, the vPMC exhibited no further increase in activity, indicating that the brain may have adapted to the lack of movement. This adaptation suggests that the system recognizes the inability to execute movement with the immobilized hand, leading to altered predictions about motor outcomes; consequently, the absence of movement becomes an expected result and the comparator system stops issuing alerting signals. Additionally, the motor threshold for the immobilized limb was found to be elevated after one week of immobilization, further illustrating the neural adaptations associated with prolonged disuse (Garbarini et al., 2019).

Granert et al. (2011) employed a voxel-based morphometry approach to investigate the impact of upper limb immobilization on gray matter volume and cortical excitability, as assessed through patients' responses to transcranial magnetic stimulation (TMS). Their findings revealed a reduction in gray matter in the primary motor cortex corresponding to the immobilized limb, which was associated with decreased cortical excitability. Notably, when patients were encouraged to increase hand activity over an eight-week period, these effects were reversed, leading to improvements in both regional gray matter volume and motor cortex excitability. The authors highlighted this phenomenon as "activity-driven bi-directional plasticity," emphasizing its functional significance, as the structural changes were paralleled

by alterations in regional excitability. This research underscores the brain's remarkable ability to recover structurally following periods of disuse (Roberts et al., 2007), demonstrating that motor activity can effectively restore both cortical volume and function.

In summary, limb immobilization induces significant neuroplastic changes characterized by decreased motor performance and alterations in corticospinal excitability. Studies have shown that even short periods of immobilization can lead to declines in voluntary muscle activation and structural changes in the brain, particularly in the primary motor cortex. Notably, these changes can be reversed through reactivation of motor activity, highlighting the brain's capacity for recovery.

The findings underscore the importance of early interventions to mitigate the negative effects of immobilization and promote functional recovery. The role of rehabilitation is, therefore, to effectively intervene in the spontaneous processes that the system will initiate due to its inherent capacity for adaptation.

Variability in research outcomes emphasizes the need for standardized methodologies in future studies to better understand the mechanisms of neuroplasticity in response to disuse.

2.2 Neuroplasticity-based rehabilitation approaches: implications for the rehabilitation

Considering all the studies described thus far within this framework that examines the effects of immobilization on the nervous system of healthy volunteers and the potential to mitigate these effects through targeted interventions aimed at preventing or reversing maladaptive plasticity, how can we justify rehabilitating only a specific group of muscles or a single joint?

In the management of fractures, physiotherapists play a pivotal role in preventing and mitigating maladaptive neural reorganization, which can impede functional recovery. Early mobilization, combined with carefully designed and supervised exercise protocols, is essential for preserving range of motion and muscular strength (Hoyt et al., 2015).

Most of the studies available in the literature have focused on the phenomenon of functional loss in the upper limb, due to its greater involvement in daily activities (Roby-Brami et al., 2021; Aderinto et al., 2023). These studies have demonstrated that a reorganization of movement is necessary, allowing for functional compensation through increased activation of the contralateral limb, as seen in tasks such as personal hygiene, cooking and other similar activities. (Winstein et al., 2003)

The lower limb recovery is “a common but complex problem” (Hoyt et al., 2015) from the rehabilitative standpoint, with recovery typically beginning once weight-bearing and full range of motion are permitted. Consequently, the restoration of function is often perceived as more straightforward. However, the functionality of the lower limbs is primarily assessed through tasks involving balance (Yoo et al., 2022), postural transitions (Ferdowsi et al., 2018) and gait (Raza et al., 2024). These tasks require coordinated involvement of both lower limbs in managing the base of support and, consequently, maintaining stability. This dual-limb coordination is critical for effective rehabilitation, as it ensures that both limbs contribute to the dynamic processes necessary for stable and efficient movement. Therefore, the complexity

of tasks involving bilateral coordination and balance highlights the importance of a comprehensive approach to lower limb functional recovery (Promsri, 2022).

In the rehabilitation of degenerative or acquired central nervous system disorders, research on exercise-induced neuroplasticity is increasingly emphasizing the need for targeted rehabilitation to promote these processes.

Since the pioneering work of V.S. Ramachandran (Ramachandran et al., 1996) on neuroplasticity, research in rehabilitation has increasingly focused on leveraging the brain's capacity to reorganize and adapt in response to injury. Ramachandran's studies, particularly his work on phantom limb pain and mirror box therapy, demonstrated that the brain retains a remarkable ability to rewire itself, even after significant trauma. Building on these insights, contemporary research has explored neuroplasticity-based rehabilitation techniques across a range of neurological conditions, including stroke, spinal cord injury and neurodegenerative diseases.

Constraint-Induced Movement Therapy (CIMT) is a specialized rehabilitation technique aimed at improving the functional use of an affected limb by restricting movement of the unaffected limb. By forcing the use of the impaired limb, CIMT helps to counteract the learned nonuse phenomenon.

The therapy involves structured and repetitive practice of motor tasks with the affected limb, which not only improves motor function but also stimulates neural pathways associated with movement and coordination. Studies have shown that CIMT can lead to significant improvements in strength, dexterity and overall functional independence. Additionally, the intensive nature of the therapy accelerates the brain's adaptive responses, reinforcing the use of the affected limb in daily activities. The long-term goal of CIMT is not only to restore

movement but also to integrate the affected limb into the patient's daily routine, improving overall quality of life (Taub et al., 1999).

Robot-assisted therapy utilizes robotic devices to support and guide movement during rehabilitation. These devices can provide fine control, repetitive practice and facilitate neuroplasticity through task-specific training (Lo et al., 2010). As of today, robot-assisted therapy is undergoing further evolution through the integration of machine learning, which enables a precise understanding of gait analysis and recognition of action intention. This advancement allows for optimized movement control (Zhang et al., 2024).

Kwakkel et al. conducted a meta-analysis showing that robot-assisted therapy significantly improves motor recovery in stroke patients compared to conventional therapy (Kwakkel et al., 2008). The repetitive, goal-directed practice provided by robotic devices enhances synaptic plasticity and cortical reorganization, leading to improved motor outcomes.

Transcranial Magnetic Stimulation (TMS) is a non-invasive technique that uses magnetic fields to promote modifications in the brain activity. TMS can modulate cortical excitability and facilitate neuroplastic changes, making it a valuable tool for enhancing rehabilitation outcomes (Rossi et al., 2004).

Transcranial magnetic stimulation (TMS) has gained recognition as a valuable complement to conventional rehabilitation, offering potential to enhance motor recovery in stroke patients. Repetitive TMS (rTMS) has been shown to improve motor function by increasing excitability in the motor cortex and promoting functional reorganization, supporting neural recovery (Kim et al., 2006). The therapeutic effects of repetitive Transcranial Magnetic Stimulation are thought to be mediated through the modulation of cortical excitability and the facilitation of practice-dependent plasticity; when integrated with physical therapy, rTMS can amplify rehabilitation outcomes, contributing to greater functional recovery. (Paquette & Thiel, 2012). Research demonstrates that applying TMS during motor practice accelerates skill

acquisition and stimulates neuroplasticity in motor learning networks (Narayana et al., 2014). Notably, low frequency rTMS targeting the unaffected hemisphere, when combined with physical therapy, has resulted in significant improvements in upper limb motor function, cognitive abilities and overall functional independence in chronic stroke patients, compared to physical therapy alone (Aşkın et al., 2017).

Mirror therapy is a rehabilitation technique that utilizes visual feedback from a mirror to create the illusion that the affected limb is functioning normally by reflecting the movements of the unaffected limb. By observing the mirror image, the brain perceives the impaired limb as moving in a coordinated and controlled manner, despite any limitations in its actual movement. This visual illusion engages the brain's mirror neuron system and leverages its ability to integrate sensory feedback from visual stimuli, which is crucial for motor learning and recovery. Through this process, mirror therapy promotes neuroplasticity, facilitating the reorganization of neural circuits responsible for movement and sensory perception. This technique has been shown to be effective in improving motor function, reducing pain and restoring a sense of control over the affected limb, particularly in patients recovering from stroke, amputations, or other neurological injuries (Deconinck et al., 2014).

Building on the observation of others' actions, rather than one's contralateral limb as in mirror therapy, is the Action Observation Therapy (AOT). It is another rehabilitative strategy that harnesses the power of action observation to promote motor recovery in patients with motor disabilities, such as those who have experienced a stroke or traumatic brain injury. This therapy is grounded in the principle that observing actions performed by others activates brain areas associated with the execution of those same actions (Buccino et al., 2001), thereby facilitating the relearning of motor skills (Sarasso et al., 2015). During AOT sessions, patients watch videos or physical demonstrations of specific motor tasks, which stimulate their premotor cortex and mirror neurons (Gallese et al., 1996) involved in motion processing and

understanding motor intentions (Zhang et al., 2018). Studies have shown that AOT can significantly improve upper limb functionality and sensorimotor integration, leading to a more rapid and effective recovery compared to traditional methods (Buccino, 2014).

Further progression stemming from implicit information processed through observation to explicit processing is found in motor imagery.

Motor imagery practice involves mentally rehearsing movements without actual physical execution (de Lange et al., 2006) and has been a topic of discussion within sports and exercise psychology (Moran et al., 2011). Studies indicate that motor imagery engages neural pathways similar to those activated during actual movement, particularly within the parieto-frontal network, which is shaped by biomechanical factors and body posture (de Lange et al., 2006). The prefrontal cortex, in conjunction with its extensive connections to the basal ganglia, plays a pivotal role in maintaining and sustaining dynamic motor representations during the motor imagery process (Decety, 1996).

These techniques can activate similar neural pathways as actual movement, promoting neuroplastic changes (Avanzino et al., 2015).

Motor imagery is a valuable method for studying motor representations, with recent advancements enhancing our understanding of its functional equivalence to actual motor action (Grezes and Decety, 2001). Effective motor imagery requires prior physical ability to execute the action (Olsson and Nyberg, 2010), as research shows that specific brain regions are crucial for generating mental movement representations (Sirigu et al., 1996). The brain forms a comprehensive motor representation, encompassing both the action plan and intended outcome, before executing a movement.

Three key aspects of motor imagery are: the perspective (first-person vs. third-person), task complexity and the role of physical experience. The first-person perspective emphasizes the internal experience of the action, while task complexity can affect the neural overlap

between imagery and action. Familiarity with a task enhances this overlap, as evidenced by distinct brain activation patterns observed in experienced individuals compared to novices (Olsson and Nyberg, 2010). Motor imagery and mental practice in motor rehabilitation can enhance motor performance (Slimani et al., 2016) and neural activation patterns, even when patients are unable to participate in physical practice due to impairments (Rannaud Monany et al., 2022).

Cognitive Multisensory Rehabilitation (CMR) (Winckel et al., 2020) is a comprehensive rehabilitative approach designed to enhance both sensorimotor and cognitive functions across various patient populations. A key aspect of CMR is its focus on the representation of movement, which encompasses not only the motor program but also the anticipated consequences of that movement.

Research has shown that CMR can lead to significant improvements in upper limb motor function, stereognosis and activities of daily living in chronic stroke patients. These enhancements are thought to arise from the restoration of connectivity within the parietal operculum, a brain region crucial for integrating sensory information and coordinating motor actions (Winckel et al., 2020).

CMR demonstrates benefits that are comparable to, or even exceed, those of other therapeutic interventions in improving upper limb functionality, gait, balance and overall quality of life in patients with neurological and traumatic conditions (del-Cuvillo-Yges et al., 2022). Its effectiveness lies in its multisensory integration, allowing patients to engage various cognitive and sensory pathways that support the rehabilitation process.

2.3 Neuroplasticity-based rehabilitation approaches in orthopedic patients

Literature increasingly highlights the need for studies that support the use of rehabilitation strategies to promote cortical reorganization following fractures or, at least, maintain function during the acute post-fracture or post-surgical period.

An example of this interest in preventing motor performance decline due to non-use during limb immobilization is provided by De Marco's study (De Marco et al., 2021). Researchers proposed action observation as an early intervention strategy to preserve motor function during periods of limb disuse, potentially decreasing the necessity for extensive motor rehabilitation in subsequent stages. By sustaining central-to-peripheral interactions that mimic the pre-injury state, Action Observation Therapy (AOT) appears to facilitate a more rapid recovery of motor abilities (De Marco et al., 2021).

The study by Bellelli and colleagues reported the effects of an action observation treatment in conjunction with physiotherapy in orthopedic patients following surgical intervention for hip fracture or hip or knee replacement. Their results strongly support the top-down effects of this treatment on motor recovery, even in non-neurologic patients (Bellelli et al., 2010).

Debarnot and colleagues (Debarnot et al., 2020) suggest the use of motor imagery practice during limb immobilization in healthy subjects to prevent the detrimental effects of immobilization on sensorimotor representation and motor cortex excitability, as assessed through the use of transcranial magnetic stimulation (TMS).

In another study (Bassolino et al., 2014) aimed at assessing the effectiveness of action observation and motor imagery interventions in healthy subjects, evidence regarding alternatives to training for patients after immobilization was provided. It was observed that after 10 hours of immobilization, action observation therapy (AOT), but not motor imagery (MI), prevented the corticomotor depression induced by immobilization. The results

demonstrate the existence of a visuomotor mechanism in humans that links action observation and execution, which can positively influence cortical plasticity (Bassolino et al., 2014).

Rannaud Monany's narrative review (Rannaud Monany et al., 2022) examines the effects of immobilization-induced hypoactivity on the brain, while also exploring the rehabilitative potential of motor imagery (MI) and action observation therapy (AOT). The review highlights that both MI and AOT involve the mental simulation of movements or the observation of actions. They can activate motor-related brain regions, thereby mitigating the adverse effects of immobilization on motor networks. The review advocates for the incorporation of MI and AOT into rehabilitation programs to stimulate cortical activity, promote motor recovery and reduce deficits associated with prolonged hypoactivity. (Rannaud Monany et al., 2022).

In conclusion, the findings highlight the value of incorporating cognitive motor interventions alongside conventional physical therapy to maximize rehabilitation outcomes post-immobilization and facilitate functional recovery by engaging neural pathways associated with movement.

The effectiveness of neuroplasticity-based rehabilitation approaches has been supported by numerous studies. Neuroplasticity-based rehabilitation approaches offer promising strategies for enhancing recovery by leveraging the brain's ability to adapt and reorganize. The integration of techniques such as mirror therapy and motor imagery into rehabilitation protocols could significantly improve functional outcomes and support neural recovery. Continued research and development are essential for optimizing these approaches and advancing our understanding of neuroplasticity in rehabilitation.

Objectives of the Present Dissertation

The overarching objective of this research is to identify and evaluate rehabilitation strategies capable of minimizing the negative consequences of immobilization following lower limb fractures and surgical interventions. The studies aim to support functional recovery by preserving central motor control and promoting early reintegration of the affected limb into postural and locomotor tasks.

To address this goal, the research employs a multimodal approach that includes:

- Comparative clinical studies examining early versus delayed weight-bearing protocols.
- Integration of technological tools, such as an antigravity treadmill combined with non-immersive virtual reality, to enable safe movement during early recovery phases.
- Implementation of cognitive strategies, such as motor imagery, to maintain cortical activation during periods of restricted physical activity.
- Comprehensive outcome assessment, combining self-reported functional measures with advanced motion analysis to evaluate load distribution and motor control during both static and dynamic tasks.

This integrated approach allows for a deeper understanding of how different rehabilitation modalities affect recovery trajectories, with the ultimate aim of improving patient outcomes and informing evidence-based clinical guidelines.

Considering the substantial impact that even a one-month period of non-weight-bearing and cast immobilization can have on patients with lower limb fractures, it is essential to develop rehabilitation strategies aimed at mitigating the negative consequences of immobilization and

enhancing functional recovery. In response to this clinical challenge, orthopaedic surgical approaches have increasingly adopted fixation techniques that allow for immediate postoperative weight-bearing on the affected limb.

The first phase of this research project (**Study 1**) aims to investigate the effects of different postoperative weight-bearing protocols on recovery outcomes following surgical fixation of lower limb fractures. Specifically, this observational cohort study compares patients following an *Early Weight Bearing* (EWB) protocol to those prescribed a *Restricted Weight Bearing* (RWB) regimen. Early weight bearing initiates weight-bearing immediately after surgery. The Restricted Weight Bearing regimen prescribed absence of weight bearing for a period ranging from 4 to 12 weeks, in accordance with established regional healthcare system guidelines.

The study assessed differences in functional recovery and interlimb load distribution using self-reported questionnaires and instrumented motion analysis during both static and dynamic tasks. The primary objective was to evaluate whether early weight bearing promotes a more favorable functional trajectory and limb reintegration during recovery.

Recognizing that not all patients are eligible for early weight-bearing protocols, the second phase of the project aimed to explore rehabilitation strategies for individuals with partial or complete weight-bearing restrictions, particularly during the acute recovery phase. These strategies were designed to preserve cortical motor activation and prevent maladaptive neuroplastic changes that can impair long-term function.

Study 2 focuses on patients with surgically treated complex lower limb fractures who are restricted from weight-bearing during the early postoperative period. The objective of this

study is to explore an early rehabilitation protocol augmented with the use of an antigravity treadmill combined with non-immersive virtual reality in functional recovery compared to traditional physiotherapy alone.

The antigravity treadmill enables walking-like movements without applying mechanical load to the affected limb, potentially allowing for early activation of gait patterns despite weight-bearing restrictions. The intervention group began this technology-assisted therapy as soon as clinical stability was achieved, while the control group followed a standard physiotherapy program.

To evaluate the impact of the intervention, both groups were assessed using validated self-reported questionnaires and motion analysis, focusing on functional performance and load distribution during static and dynamic tasks. The strategy behind this approach was to introduce a safe form of early mobilization capable of stimulating neuromotor pathways and promoting more physiological gait recovery. The study aims to determine whether the use of this technology could accelerate the return to daily activities, facilitate earlier reintegration of normal gait patterns and reduce compensatory mechanisms typically associated with prolonged unloading.

Study 3 involves a separate cohort of patients with lower limb fractures managed conservatively through cast immobilization and complete weight-bearing restriction. The objective of this pilot study is to investigate whether motor imagery (MI), a cognitive strategy involving the mental simulation of movement, can serve as an effective adjunct to conventional physiotherapy in preserving motor control during periods of immobilization.

The strategic rationale for employing MI lies in its potential to maintain cortical motor representations and mitigate maladaptive neuroplastic changes that can occur during prolonged inactivity. Patients in the experimental group perform structured MI exercises alongside

standard physiotherapy during the immobilization period, while a matched control group receive only conventional physiotherapy.

To evaluate the effects of this intervention, functional recovery, movement perception and interlimb load distribution are assessed using validated self-administered questionnaires and motion analysis performed during specific static and dynamic tasks. The study aims to determine whether early integration of MI can help preserve motor control, limit disuse-related deficits and facilitate a smoother and more rapid return to full functional activity once physical mobilization becomes possible.

In the final chapter, the studies presented in this thesis are discussed as complementary approaches for managing patients with lower limb fractures who, due to temporary functional limitations, experience significant restrictions in their ability to engage in social, occupational and recreational activities. Rather than a direct comparison, each study offers a distinct perspective on how to support recovery during periods of non-weight bearing or immobilization, highlighting possible strategies for reducing inactivity-related impairments and promoting earlier reintegration into daily life.

The previous chapters outlined evidence from the literature on cortical reorganization and muscular adaptations following immobilization. Building upon this foundation, the studies conducted as part of this research project examine how different rehabilitation protocols influence motor recovery and load distribution during functional static and dynamic tasks such as standing, walking initiation and sit-to-stand transitions. These outcomes were measured after an initial rehabilitation phase in which all patients had resumed weight-bearing, using validated self-report questionnaires and motion analysis to assess both subjective recovery and objective motor function.

The aim of this thesis is to propose viable rehabilitative strategies tailored to patients with varying levels of post-fracture mobility restrictions, emphasizing individualized care approaches that can reduce the burden of inactivity and support functional restoration. The findings also consider the feasibility and acceptability of the proposed interventions, which received positive feedback from the participating patients, particularly in terms of engagement and perceived usefulness.

“Bisogna pensare al movimento, non al muscolo. Dopo tutto, la gente si muove, "fa" le cose, non tende i muscoli.”

“One needs to think of a movement, not a muscle. After all, people move, they do things, they don't tense their muscles.”

Oliver Sacks, A Leg to Stand On

Chapter 3 - Experimental Section

3.1 General Methods

For the studies presented in the second part of this dissertation, the Motion Analysis Laboratory of the Physiotherapy Bachelor's Degree Program at the University of Trieste is utilized. The motion analysis evaluation protocol is applied consistently across all the proposed studies.

3.1.1 Ground Reaction Forces in orthopedic assessment and rehabilitation

Ground reaction forces (GRFs) constitute a critical kinetic parameter extensively utilized for the comprehensive evaluation of gait and functional recovery in orthopedic populations (Wang et al., 2024; Hecht et al., 2022). Unlike clinical observation, patient-reported outcomes, or purely kinematic analyses, kinetic data provide essential insights into the mechanical loads experienced by the musculoskeletal system, thereby enabling a more accurate assessment of patient function (Hecht et al., 2022) and facilitating the design of individualized postoperative rehabilitation protocols (Kadaba et al., 1990).

Kammerlander et al. (2018) highlighted that older adults sustaining hip fractures frequently exhibit substantial impairments in physical performance that may not be fully captured by conventional functional assessments or subjective reports. Objective kinetic measures such as GRFs, joint moments and joint power could allow for a quantification of these deficits, revealing subtle alterations in movement quality that remain undetected by kinematic or temporal-spatial analyses alone. This distinction is crucial because while kinematics describe the pattern of movement, kinetics elucidate the underlying forces and moments responsible for these patterns (Whittle, 1996). For example, individuals with comparable kinematic profiles may adopt distinct biomechanical strategies, which can impose

excessive loads on joints or soft tissues or reflect underlying muscular weaknesses (Falisse et al., 2019).

Hecht et al. (2022) further emphasized the enduring clinical relevance of gait analysis in orthopedics, underscoring that kinetic data are indispensable for understanding the mechanical environment of musculoskeletal structures. These data are useful not only for diagnostic purposes but also for surgical planning, where evaluation of joint loading informs implant selection, alignment correction and perioperative muscle strengthening to optimize patient outcomes (Hecht et al., 2022).

Kinetic analysis facilitates the detection of asymmetrical joint loading and compensatory load redistribution that may persist even when kinematic gait patterns appear normalized (Christensen et al., 2021). Such imbalances increase mechanical stress on contralateral joints, thereby elevating the risk of osteoarthritis and other degenerative sequelae (Savage et al., 2025; Aljehani et al., 2022). Abnormal gait, characterized by deviations in temporal-spatial, kinematic, kinetic, or muscle activation parameters, has been implicated in the degeneration of articular cartilage, particularly within the knee joint, leading to diminished vertical GRF absorption and accelerated onset of post-traumatic osteoarthritis (Farrokhi et al., 2011).

Typically, GRFs are measured using force plates embedded within motion analysis laboratories, which generate force-time curves that are both accurate and readily interpretable (Vaverka et al., 2015; Hecht et al., 2022). Although force plates remain the gold standard, emerging technologies such as piezoelectric sensors and instrumented insoles are expanding the capacity for portable and ecological GRF assessment, enabling long-term monitoring outside laboratory environments (Shahabpoor et al., 2018). For instance, instrumented insoles have demonstrated reliability in capturing GRF parameters during early rehabilitation

following tibial fractures, offering advantages over traditional methods by reducing dependence on spatiotemporal coherence (Wolff et al., 2025).

Conceptually, the GRF vector represents the force exerted by the body (typically the foot) on the ground, encompassing both magnitude and direction. This vectorial characterization allows detailed biomechanical analyses of dynamic interactions between the body and support surface during gait and other functional tasks (Marasovic et al., 2009).

Correlations between GRF parameters and joint range of motion (ROM) have been reported: ankle dorsiflexion ROM is associated with various GRF components during gait, highlighting the biomechanical interplay between joint mobility and force generation (Fong et al., 2011; Almansoof et al., 2023). Limited ankle dorsiflexion impairs plantarflexor power during push-off, which is critical for effective propulsion and gait velocity (Lamontagne et al., 2002; Aquino et al., 2024).

Despite these promising insights, limitations such as small sample size and technical constraints, including force plate dimensions and positioning, must be acknowledged. Controlled laboratory conditions may not fully replicate natural gait patterns, underscoring the need for further research utilizing wearable sensors and ecological monitoring to validate and extend these findings (Najafi et al., 2011).

In conclusion, kinetic analysis through GRF measurement provides biomechanical data that complement kinematic and clinical assessments. Integrating kinetic insights into orthopedic rehabilitation enhances understanding of gait impairments, guides personalized interventions and contributes to improved patient outcomes.

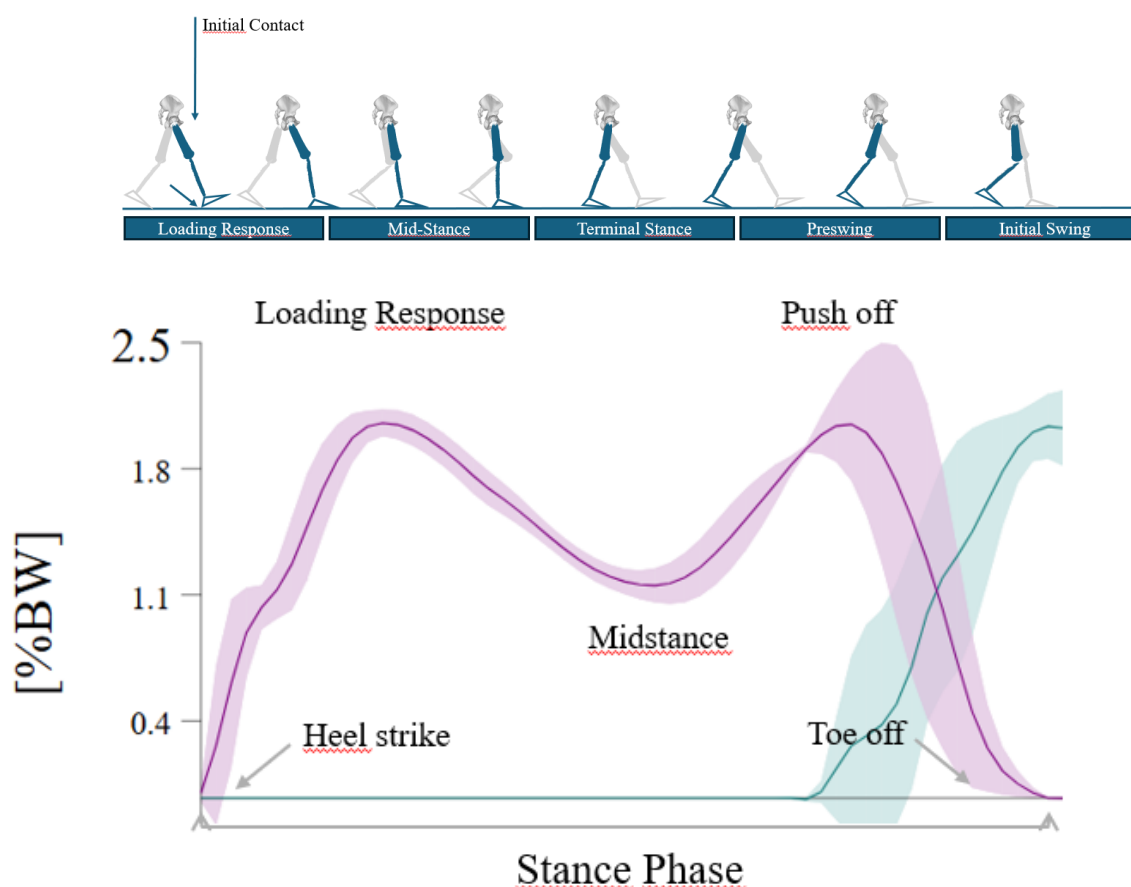
3.1.2 Qualitative analysis of Ground Reaction Forces in clinical gait assessment

In clinical settings, ground reaction forces (GRFs) are frequently assessed through qualitative means, as the visual inspection of force-time curves can provide clinicians with rapid and reliable insights into gait deviations (Vaverka et al., 2015). By examining these curves, clinicians can quickly identify salient features such as the magnitude and timing of the vertical (F_z), anterior-posterior (F_y) and mediolateral (F_x) GRF components, which reflect fundamental aspects of gait mechanics including weight acceptance, propulsion and balance (Chockalingam et al., 2016; Vaverka et al., 2015). The characteristic double-peaked vertical GRF curve readily highlights the loading response and push-off phases of gait. Deviations observed in the anterior-posterior GRF component may indicate braking or propulsive deficits commonly associated with pathological gait patterns (Chockalingam et al., 2016; Vaverka et al., 2015). While the mediolateral GRF component is inherently more variable, it offers clinicians qualitative information regarding frontal plane stability and the specific balance strategies employed by the individual (Rawal et al., 2021; Vaverka et al., 2015).

The advantage of this qualitative approach is its efficiency and ease of use, enabling clinicians to screen for gait abnormalities without requiring complex post-processing or advanced computational techniques. Nonetheless, a qualitative assessment should ideally be complemented by quantitative analyses to more precisely detect subtle impairments and to monitor changes over time (Ferber et al., 2003; Vaverka et al., 2015). The visualization and interpretation of GRF curves serves as a valuable clinical tool that can inform further diagnostic evaluations and guide the development of targeted therapeutic interventions.

GRFs are often collected using force plates that are integrated into the floor of motion analysis laboratories, enabling the generation of force-time curves (Vaverka et al., 2015).

Figure 1 – Graphical representation of the GRFs in $f(z)$ during stance phase in gait circle.



3.1.3 Assessment of Ground Reaction Forces using Force Plates

Force plates are widely utilized to measure ground reaction forces (GRFs) during the stance phase of gait, defined as the period when the foot maintains contact with the ground (Mayich et al., 2013). The GRF, expressed in newtons, represents the force exerted by the ground on the foot, which, according to Newton's third law, is equal in magnitude and opposite in direction to the force applied by the foot to the ground (Mayich et al., 2013). During normal gait, GRF profiles typically exhibit a characteristic M-shaped pattern throughout the stance phase. The initial peak corresponds to forces generated at heel strike, while the second peak

reflects forces during heel rise and toe-off. The intervening trough represents the midstance phase, characterized by a transition of force from the heel to the forefoot and relatively lower force levels (Mayich et al., 2013). Evaluating GRFs is critical for gait performance analysis, as various foot and ankle pathologies produce distinctive deviations from normative GRF patterns (Mayich et al., 2013).

Despite the clinical importance of GRF curve analysis, there is a lack of dedicated commercial software tailored specifically for this purpose; consequently, researchers often develop custom analysis tools to meet the demands of individual studies (Vaverka et al., 2015). The selection of temporal and kinetic variables derived from GRF data depends on the specific gait characteristics under investigation. The vertical component of the GRF (F_z), which acts perpendicular to the ground and counteracts gravitational forces, is frequently emphasized due to its high magnitude and relevance (Fortin et al., 2008; Vaverka et al., 2015). Peaks in both the vertical and anteroposterior components are commonly analyzed as they correspond to ground impact and propulsion phases during gait (Fortin et al., 2008; Vaverka et al., 2015).

Force plates measure GRFs in three orthogonal directions: mediolateral (F_x), anteroposterior (F_y) and vertical (F_z). The mediolateral component plays a pivotal role in maintaining balance within the frontal plane, while the anteroposterior component influences gait velocity through acceleration and deceleration mechanisms (Fortin et al., 2008; Peterson et al., 2011). Observations of GRF patterns reveal that F_x typically exhibits a single peak in medial and lateral directions, F_y shows a single peak during braking and propulsion and F_z displays two maxima separated by a minimum, consistent with the phases of stance (Fortin et al., 2008; Vaverka et al., 2015).

Figure 2 – Visualization of GRF in $f(z)$: vertical forces during the stance phase (both limbs).

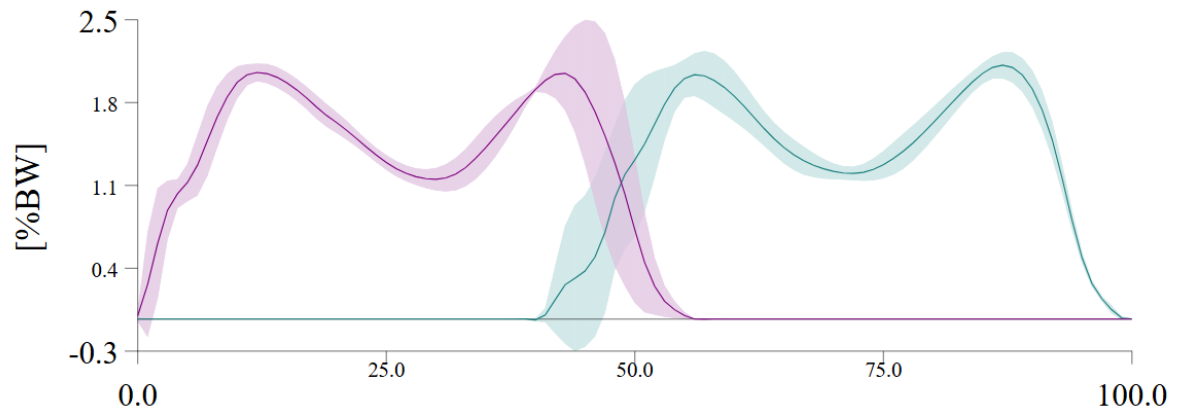


Figure 3 – Visualization of GRF in $f(y)$: vertical forces during the stance phase (both limbs).

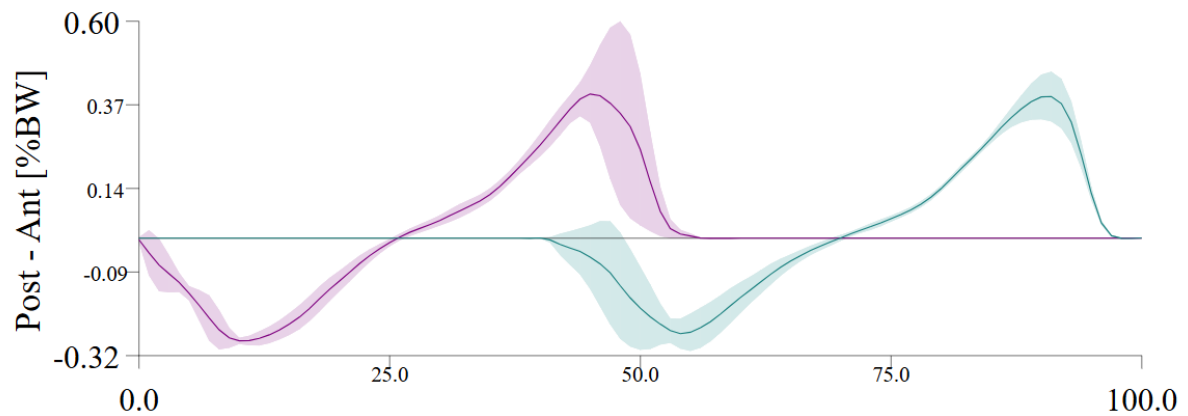
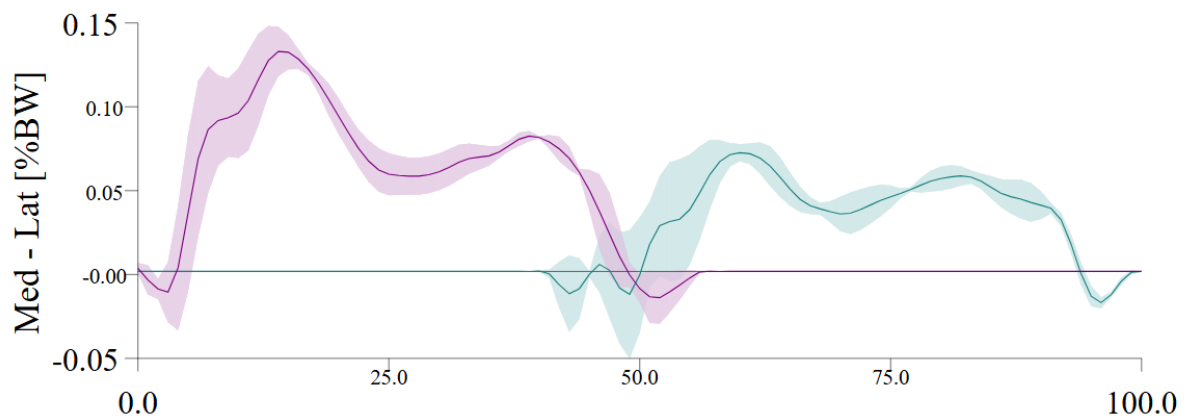


Figure 4 – Visualization of GRF in $f(x)$: vertical forces during the stance phase (both limbs).



3.1.4 Study Protocol: functional evaluation of Ground Reaction Forces across static and dynamic tasks

The studies described in the next chapters analyze ground reaction force (GRF) components not only during gait but also across a variety of tasks designed to replicate activities of daily living, with the goal of assessing the functional outcomes of surgical and rehabilitation interventions.

To explore how GRFs vary under different sensory and postural conditions, four static standing tasks are implemented:

- Standing with eyes open
- Standing with eyes closed
- Standing with arm abducted and eyes open
- Standing with arm abducted and eyes closed

Participants are instructed to maintain a stable stance on the force platforms for at least 10 seconds, initially with eyes open and subsequently with eyes closed. To examine the influence of upper limb positioning on postural control, subjects abduct the arm on the same side as the injury and hold this posture for a minimum of 10 seconds under both visual conditions (Shumway-Cook & Woollacott, 2001; Santos & Aruin, 2009; Mancini et al., 2012). These manipulations are well-established for investigating sensory integration and balance control, with GRF measurements providing quantitative insight into postural stability and compensatory mechanisms.

Dynamic assessments include the following tasks:

- Sit-to-stand
- Rise-to-walk
- Gait initiation
- Walking

For the sit-to-stand task, participants begin seated on a bench without armrests or backrests, hips flexed at 90°, positioned directly in front of the force platforms with both feet resting comfortably on the plates. Upon a verbal cue and after recording commences, participants rise to a standing position and maintain upright posture. To reduce variability caused by arm movement, subjects are instructed to place their hands on their hips (Galli et al., 2008; Bohannon, 1995).

The rise-to-walk task extends this movement by requiring participants, after standing, to initiate walking along a designated walkway at a self-selected pace, starting their first step on the second force platform (Jones et al., 2018).

During gait initiation, participants stand with feet positioned on adjacent force platforms and begin walking naturally without external prompting, initiating movement with the operated limb (Park et al., 2009).

In the walking task, subjects ambulate along a 10-meter by 1.3-meter path at their preferred speed. Only the steps occurring on the force platforms are analyzed to capture representative GRF data (Horst et al., 2021).

All tasks are performed at self-selected speeds to reflect participants' natural movement patterns. Prior to data collection, subjects complete several practice trials to ensure familiarity with the procedures. Each task is repeated three times to allow for averaging and to enhance measurement reliability.

The chosen static and dynamic tasks are supported by extensive literature demonstrating their relevance for evaluating functional recovery in orthopedic and rehabilitation settings. Standing tasks with variations in visual input and arm position are commonly used to probe sensory contributions to balance and postural control, as well as the

biomechanical effects of upper limb positioning, with GRF data serving as a sensitive measure of these factors (Sozzi et al., 2023; Cheng et al., 2015; Shumway-Cook & Woollacott, 2001).

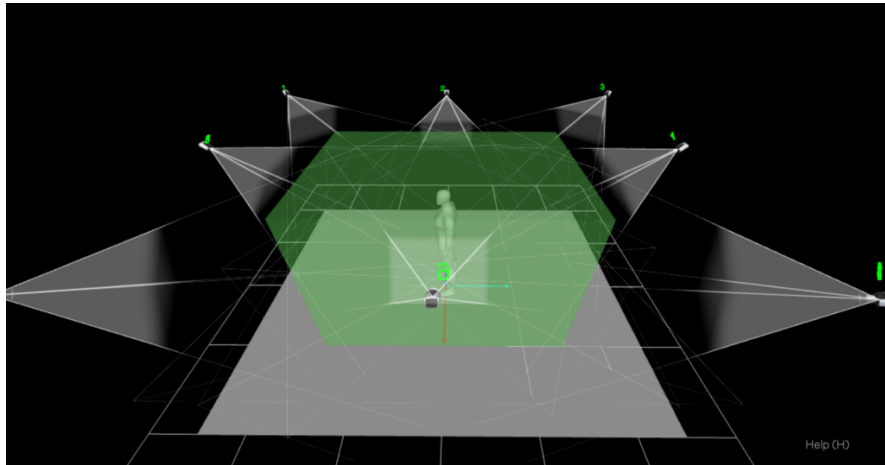
Dynamic tasks such as sit-to-stand and rise-to-walk are widely recognized as functional indicators of lower limb strength and balance, with GRF patterns reflecting progress in post-surgical recovery (Houck et al., 2011; Jones et al., 2020). Gait initiation is particularly sensitive to detecting motor control deficits, revealing anticipatory postural adjustments and propulsion impairments through GRF analysis (Anand et al., 2017). Continuous gait assessment during walking captures biomechanical changes associated with orthopedic interventions, providing insight into functional status (Wang et al., 2024).

3.1.5 The Motion Analysis Laboratory

All tasks are performed barefoot along a 10-meter walkway in the instrumental gait analysis laboratory, equipped with eight high-speed infrared cameras (Qualisys System Cameras - Qualisys AB, Göteborg, Sweden Oqus +7, 4MP, 180 fps) to track the position and movement of 25 reflective markers. The camera system is calibrated before each data collection. Four contiguous force platforms (BTS P-6000, each measuring 60x40cm) are positioned centrally and longitudinally along the walkway to record kinetic data. Data obtained from the force plates provide information regarding ground reaction forces (GRFs).

Figure 5 – Virtual rendering of the motion analysis laboratory acquisition space with 8 cameras.

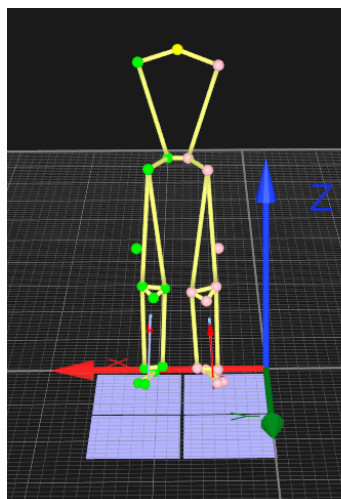
Copyright: Qualysis Lab Designers



Twenty-five reflective passive markers are placed directly onto the participants' bodies using double-sided tape, following a modified Helen Hayes model with greater emphasis on the pelvic and lower-extremity segments (Leardini et al., 2007), based on anatomical reference points (see Figure 6 for details).

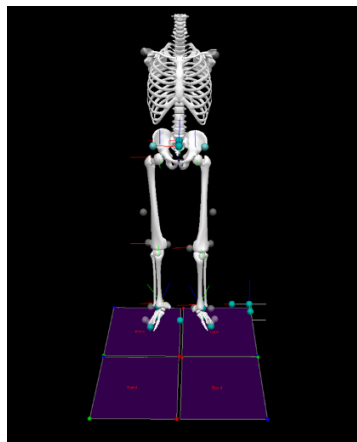
The positions of the 3D markers are used both to define the size and orientation of each body's segment and to track the movement of these segments.

Figure 6 – 25 passive markers position according to modified Helen Hayes protocols and acquisition using Qualysis Capture System for model reconstruction.



Data are processed using Qualisys Track Manager software (version 2.7). Subsequently, all data were analyzed using Visual 3D™ software (C-Motion, Inc., Germantown, USA). Vertical ground reaction forces are normalized to body mass and based on the length of each individual patient's limb, using analysis performed with Visual3D software.

Figure 7 – Presentation of the anatomical model for data processing in Visual 3D software.



3.1.6 Data measurement: assessment of postoperative joint function and rehabilitation outcomes

Joint function recovery following surgical intervention is systematically evaluated throughout the rehabilitation process and at its conclusion. Assessments are conducted at three key postoperative intervals: 6 weeks (T1), 3 months (T2) and 6 months (T3), consistent with established timelines for musculoskeletal healing and functional restoration (Chen et al., 2024; Warmerdam et al., 2023).

Functional recovery is quantified using validated, region-specific patient-reported outcome measures. For knee function, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was employed: the Italian adaptation (Salaffi et al., 2003) of the WOMAC has demonstrated reliability and validity in assessing the severity of knee

osteoarthritis, with measurement properties consistent with those of the original, widely adopted version (Bellamy et al., 1988). Ankle function is assessed using the American Orthopaedic Foot and Ankle Society (AOFAS) (Kitaoka et al., 1994; SooHoo et al., 2003) score alongside the Olerud Molander Ankle Score (OMAS) (Olerud & Molander, 1984), both demonstrating strong construct validity in postoperative contexts (SooHoo et al., 2006; Penning et al., 2023; Nilsson et al., 2007).

The Olerud-Molander Ankle Score (OMAS) is employed as a patient-reported functional rating scale ranging from 0 (totally impaired) to 100 (completely unimpaired), encompassing nine domains: pain, stiffness, swelling, stair climbing, running, jumping, squatting, use of supports and activities of daily living (Olerud & Molander, 1984). The OMAS has been extensively utilized to subjectively evaluate functional outcomes after ankle fractures (Nilsson et al., 2007).

The American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Scale is used as a clinician-administered instrument assessing pain (40 points), function (50 points) and alignment (10 points), with a total possible score of 100 points (Kitaoka et al., 1994; SooHoo et al., 2003). This scale integrates both subjective and objective clinical parameters to provide a comprehensive evaluation of foot and ankle outcomes.

The literature identifies a minimum clinically important difference (MCID) exceeding 10 points on these scales as indicative of functional improvement (Clement et al., 2018; Penning et al., 2023).

All assessments are performed according to standardized protocols to ensure reliability and reproducibility.

Progression to full weight-bearing is objectively monitored using symmetry indices derived from force plate analyses comparing the operated and contralateral limbs (Alves et al.,

2020), with asymmetry values below 10% considered reflective of effective load distribution (Hodt-Billington et al., 2011; Wiik et al., 2017).

Joint range of motion (ROM) is assessed by skilled physical therapists following a standardized measurement protocol that employed a long-arm goniometer. It is well established that the accuracy and consistency of goniometric measurements depend more on the precision of the measurement technique than on the specific instrument utilized (Hancock et al., 2018). To ensure reliable and reproducible results, patients are positioned on adjustable examination tables, which facilitated optimal comfort and stabilization during assessment.

Key procedural steps include the identification of anatomical landmarks and alignment of the goniometer arms with these reference points, for minimizing variability between measurements and across different evaluators (Lenssen et al., 2007; Hancock et al., 2018). Prior to data collection, clinicians received training to ensure uniform application of the protocol, a factor that contributes to the high inter-rater reliability reported in the literature, with intraclass correlation coefficients (ICC) exceeding 0.85 when measurements are performed by experienced practitioners (Gogia et al., 1987; Jakobsen et al., 2010). The use of a long-arm goniometer is advantageous in measuring larger joint angles due to its extended lever arm, which enhances alignment accuracy with anatomical axes and improves measurement precision (Hancock et al., 2018).

Pain intensity is assessed using the Numeric Rating Scale (NRS), a validated tool ranging from 0 (no pain) to 10 (worst imaginable pain) (Hjermstad et al., 2011; Jensen et al., 1986), where a reduction of two points or more is considered clinically significant (Salaffi et al., 2004).

In addition to region-specific functionality, assessment included time of achieving full weight-bearing (defined as the perceived weight distribution on the operated limb in standing

position), perceived independence in performing activities of daily living (ADL) and the resumption of pre-trauma sports or recreational activities.

This comprehensive, multimodal evaluation protocol aligns with contemporary consensus guidelines for postoperative orthopedic rehabilitation, integrating objective biomechanical parameters with patient-centered outcomes to holistically monitor recovery trajectories (Ayers et al., 2013).

Radiographic and clinical evaluations are conducted by the surgeons to monitor fracture healing and identify complications such as loss of reduction, hardware failure, infection, nonunion, ligamentous instability and malalignment, under the supervision of the multidisciplinary clinical team.

3.1.7 Data analysis

Data collection and storage are conducted in compliance with EU Regulation 2016/679 (GDPR), for the purposes outlined in this document. Data extraction is performed by authorized medical personnel and subsequently anonymized to facilitate analysis. All data are stored in digital workbooks on a secure, offline computer, protected by password and with access restricted exclusively to study assessors. Given the limitations in sample size and to minimize potential bias from multiple statistical analyses, the statistical evaluation is restricted to selected parametric parameters.

Statistical analysis is performed using Jamovi v.2.3.18.0, with group comparisons conducted via the Mann-Whitney U test and Fisher's exact test. A significance level of $p < 0.05$ was applied to the results of both tests.

1. Static Balance Assessment (Eyes Open/Closed and Arm Abduction)

For static balance evaluations, mean ground reaction force (GRF) values are determined for both the operated and contralateral limbs using established measurement protocols (Jørgensen et al., 2021). These measurements are performed at three postoperative time points: 6 weeks (T1), 3 months (T2) and 6 months (T3); and averaged for each session. To quantify load distribution symmetry, the following formula is applied: $(\text{GRF on operated limb} / \text{sum of GRFs on both limbs}) \times 100$ (Alves et al., 2020). This symmetry index is validated for detecting clinically meaningful asymmetries, with values below 90% indicating persistent functional deficits (Hodt-Billington et al., 2011; Wiik et al., 2017).

The minimum distance between the center of mass (COM) and the center of pressure (COP) is recorded for each trial. Lower COM-COP distances are indicative of effective postural control, while greater distances may reflect impaired balance (Paillard et al., 2015).

2. Sit-to-Stand Task

During the sit-to-stand movement, peak vertical GRF values are captured for both limbs during the propulsion phase, which is strongly associated with knee extensor strength and overall functionality (Farquhar et al., 2008; Shen et al., 2017).

3. Gait Analysis

For walking assessments, temporal parameters such as step time, average walking speed and step length are measured alongside GRF components in the vertical (fz), anterior-posterior (fx) and mediolateral (fy) directions during the stance phase for both lower limbs (Esmailpour et al., 2025). The variability of the vertical GRF (fz), calculated as the difference between its maximum and minimum values, served as an index of gait symmetry (Hosseini-Yazdi, 2024). The minimum COM-COP distance during the stance phase is also recorded.

4. Gait Initiation

In the analysis of gait initiation, GRF components (f_z , f_x , f_y) and minimum COM-COP distances are examined to assess anticipatory postural adjustments, which are frequently altered in individuals with musculoskeletal impairments (Yamada et al., 2021; Shiozawa et al., 2015). These metrics provide insight into the preparatory strategies used to initiate movement and maintain stability.

5. Rise-to-Walk Task

For the rise-to-walk task, the peak vertical GRF immediately prior to leaving the seated position is analyzed as a marker of lower limb strength. Additionally, shifts in mediolateral GRF (f_x) are evaluated to detect compensatory loading patterns, which may emerge postoperatively or in response to musculoskeletal deficits.

3.1.8 Handling of Missing Data

Statistical evaluations are carried out strictly on the available, collected data, deliberately omitting any procedures with missing values. By analyzing only records where data are complete, the conclusions are based solely on actual observations. This choice is made to reduce the risk of bias often associated with imputation techniques and to uphold the internal consistency of the research (Myers, 2000). Nevertheless, this decision could impact on the applicability of our findings to broader populations, especially if the absence of data isn't purely by chance (Myers, 2000).

3.2 Study 1. Analysis of ground reaction forces (GRFs) during static and dynamic tasks through motion analysis in patients with early weight-bearing after lower limb fractures and in patients with weight-bearing restrictions: an observational study

A portion of the data presented herein is currently under submission to the journal *Annali Italiani di Chirurgia* (ISSN/eISSN: 0003-469X/2239-253X).

Abstract

Early weight-bearing (EWB) protocols following surgical fixation of ankle and tibial plateau fractures have gained increasing attention for their potential to mitigate the negative consequences of immobilization while supporting neuromuscular and functional restoration. Despite concerns about safety and fracture healing, emerging evidence suggests that appropriately guided EWB can be safely implemented and may improve muscle preservation, gait dynamics and overall functional outcomes compared to prolonged restricted weight-bearing (RWB). This prospective study aims to compare the biomechanical and clinical outcomes of early weight-bearing (EWB) versus restricted weight-bearing (RWB) protocols on recovery following surgical fixation of ankle and tibial plateau fractures using objective gait analysis and functional assessments. Forty-eight patients meeting stringent inclusion criteria were assessed at 6 weeks, 3 months and 6 months postoperatively using validated functional questionnaires and gait analysis. No fixation failures or surgery-related complications were observed in either group. Patients in the EWB group demonstrated a trend toward faster functional recovery, including earlier independence in daily activities and return to work and sports, though differences were not always statistically significant. Gait analysis revealed subtle improvements in ground reaction force symmetry and postural control with EWB, especially during complex tasks. However, long-term functional outcomes were similar

between groups. Limitations include the small sample size and lack of blinding. Overall, findings suggest that EWB is a safe and beneficial approach, supporting its consideration in postoperative rehabilitation, while further large-scale studies are needed to confirm these results.

3.2.1 Introduction

Fractures of the lower extremity, excluding hip fractures, are among the most frequently observed musculoskeletal injuries within the adult and working-age populations worldwide. Ankle fractures have a high global incidence, approximately 168 per 100,000 individuals, with demographic trends showing a peak during adolescence and a shift toward female predominance after the age of 50 (Elsøe et al., 2018). Tibial plateau fractures, which compromise the articular surface of the proximal tibia, are less common (10.3 per 100,000), but involve greater complexity due to their intra-articular nature. These injuries tend to occur more often in younger men and postmenopausal women (Elsøe et al., 2015).

Given the impact that fractures, surgical treatment and the subsequent recovery process have on patients' quality of life, numerous studies have focused on reducing the duration of functional limitations, including autonomy in activities of daily living (ADLs), returning to work and social participation, as framed within the International Classification of Functioning, Disability and Health model (Noback et al., 2020; Baji et al., 2024; Van Son et al., 2016). These concerns are particularly relevant during the immediate post-surgical period, where decisions regarding immobilization and load-bearing have significant implications for recovery, as outlined in *Chapters 1 and 2*.

Recent developments in clinical practice, corroborated by updated AO Foundation guidelines (2024) and international literature (Bretherton et al., 2024; Kubiak et al., 2013; Haller et al., 2013), have emphasized the benefits of reducing post-operative immobilization

and promoting earlier initiation of weight-bearing. While the nature and timing of loading (touch, partial, or full weight-bearing) can vary based on fracture type, fixation stability and patient-specific factors, early mobilization is increasingly recognized as a safe and effective approach in many cases (Apisunadi et al., 2023; Meys et al., 2019). However, the final decision regarding weight-bearing protocols typically rests with the operating surgeon, who considers both radiological findings and clinical status (Bretherton et al., 2024).

To date, surgical fixation procedures for the lower limb with early weight-bearing indications are a well-established practice at the international level (Flowers et al., 2022). The weight-bearing recommendation can vary (full, partial, or in some cases touch-bearing) allowing the patient to place the foot on the ground during the initial post-operative period (Braun et al., 2017). In all cases, weight-bearing is progressively increased based on radiological evaluations and the patient's tolerance level (Meys et al., 2019). Nonetheless, more important than any guideline remains the assessment and recommendation provided by the operating surgeon at the time of surgery (Bretherton et al., 2024; Kalmet et al., 2024; Swart et al., 2015). Beyond the fracture itself, it is crucial to consider pre-fracture activity level, bone condition and any existing comorbidities (Gahr et al., 2023; Kalmet et al., 2018).

For ankle fractures without complications, early full weight-bearing is now widely accepted as standard practice (AO Foundation, 2024). On the other hand, the management of tibial plateau fractures remains more contentious. While some studies support early loading without increased complication risk (Williamson et al., 2018; Canton et al., 2022; Meys et al., 2019), others recommend a more conservative approach, delaying full weight-bearing until 9–12 weeks postoperatively (Arnold et al., 2017).

Studies evaluating these approaches (Williamson et al., 2018; Striano et al., 2022; Meys et al., 2019) have evaluated the effectiveness of early weight-bearing protocols in relation to functional outcomes, radiographic assessments and pain presence. These evaluations are

typically based on specialist reviews of radiological images to determine fracture healing timelines post-surgery, as well as functional questionnaires completed by patients during orthopedic follow-ups. These outcomes have demonstrated the benefits of weight-bearing in the fracture healing process, showing no increase in complications (which occur at a similar rate to cases where weight-bearing restrictions are applied) and a reduction in the time needed to return to normal daily activities (Smeeing et al., 2015; Flowers et al., 2022).

This method of data collection, which provides a comprehensive response regarding the issue of patients' return to autonomy and the success of the surgical intervention (Billing et al., 2019), does not allow for any deeper analysis of the movement or action execution assessed by the patient-reported outcome measures questionnaires (Giladi et al., 2017).

To address these limitations, biomechanical gait analysis has emerged as a valuable tool to objectively evaluate functional recovery in patients with lower limb fractures (Wang et al., 2010; Kröger et al., 2022). Spatiotemporal analyses in patients with ankle fractures have revealed decreased stance time, limited joint motion and altered load distribution, also with altered trunk mobility and knee joint limitations during the swing phase, correlating these findings with a reduction in loading time on the affected lower limb and reflecting avoidance strategies (Mirando et al., 2022). The ankle range of motion was found to be reduced in relation to the severity of the fracture (Wang et al., 2010; Mirando et al., 2022), resulting in increased load distribution laterally during loading response (Roos et al., 2017; Menz et al., 2003; Jensen et al., 2013). In tibial plateau fracture populations, similar studies have identified persistent reductions in knee extension and deviations in gait symmetry with altered sagittal kinematics extending up to three months post-injury, affecting gait efficiency (Fändriks et al., 2021).

Further investigations by Elbaz et al. (2016) and van Hove et al. (2019) on ankle fractured patients have shown persistent asymmetries in spatiotemporal parameters (reduced walking speed, asymmetrical step length) and kinetic deficits (decreased ankle push-off power

and diminished knee extension moment). Bennett et al. (2021), using a 2-year follow-up design, reported incomplete recovery of ankle and knee biomechanics following tibial plateau fractures, particularly delayed heel-off timing, even in patients classified as functionally recovered.

Kinetic parameters, particularly ground reaction forces (GRFs), provide sensitive insight into recovery progress in load transfer. Iliopoulos et al. (2020B) documented reduced single-limb support durations and asymmetric loading patterns. Recent work by Raza et al. (2024) has linked diminished GRF symmetry in the anteroposterior direction to altered limb stiffness, highlighting the utility of kinetic markers in evaluating motor control strategies. Warmerdam et al. (2023) further proposed that pedographic assessment and GRF analysis may serve as early biomarkers for fracture healing, showing that GRF alterations can reflect radiographic signs of union.

Despite the utility of gait analysis, there is a lack of standardization regarding the timing and frequency of assessments. Studies vary widely, with some initiating analysis two weeks after surgery (Bennet et al., 2021; Thewlis et al., 2015), while others conduct gait evaluations at extended intervals such as 12 months (Losch et al., 2022; Falzarano et al., 2018) or even 18 months (Hoeve et al., 2019) and 20 months (Joslin et al., 2018) post-fracture to capture long-term functional outcomes. This heterogeneity limits the ability to identify recovery patterns or predict long-term outcomes. Moreover, most studies conduct single-point assessments, thereby missing opportunities to monitor the progression of healing or detect deviations from expected recovery trajectories (Warmerdam et al., 2023).

Recent systematic reviews emphasize the need for standardized, serial gait assessments to better inform rehabilitation planning and identify at-risk individuals early in the recovery process (Rezapour et al., 2024; Warmerdam et al., 2023; Chakraborty et al., 2022). As

emphasized in Chapter 3, this lack of standardization impedes the use of biomechanical data in routine clinical decision-making. Early and repeated kinetic and kinematic evaluations may provide valuable prognostic information and guide individualized interventions.

Given these limitations, the current study aims to assess patients recovering from tibial plateau or ankle fractures using 3D motion analysis at three time points over the first six months post-surgery. The primary objective is to characterize the evolution of GRFs and load distribution patterns during static and dynamic tasks that simulate daily activities. Data may provide actionable insights into how patients manage their base of support and motor control during recovery.

This approach is expected to yield clinically relevant insights into load distribution strategies and compensatory mechanisms, contributing to the development of targeted rehabilitation protocols that support early functional reintegration into work and daily life.

3.2.2 Materials and Methods

This prospective monocentric observational study was conducted at the Orthopedic Clinic of the Department of Medicine, Cattinara Hospital-ASUGI (Azienda Sanitaria Universitaria Giuliano Isontina), affiliated with the University of Trieste. Patient enrollment began in March 2021 and continued according to the inclusion criteria outlined below.

Biomechanical and clinical assessments are performed in the Motion Analysis Laboratory of the Physiotherapy Degree Program at the University of Trieste, in collaboration with the Department of Orthopaedics and Traumatology at Cattinara Hospital. Biomechanical data are collected using an eight-camera infrared motion capture system operating at 200 Hz, synchronized with four embedded force plates. System calibration adheres to the International Society of Biomechanics (ISB) guidelines to guarantee accuracy and reproducibility (Wu et

al., 2002). Participants perform barefoot trials along a 10-meter walkway, completing a series of functional tasks including static postural control with eyes open and closed and with arm abduction, sit-to-stand and rise-to-walk transitions, gait initiation and steady-state walking. Ground reaction force (GRF) data are normalized to body mass and a symmetry index is calculated as the percentage of GRF borne by the operated limb relative to the total GRF. Further technical details regarding hardware, marker placement, data processing protocols and theoretical foundations are provided in the *General Methods* chapter.

Eligible participants are adult patients aged between 18 and 65 years who have undergone surgical fixation for isolated ankle or proximal tibial fractures. Inclusion criteria mandate radiographic and clinical confirmation of fracture and subsequent surgical stabilization. To reduce confounding variables, several exclusion criteria are applied, including fracture-dislocations, Weber C-type fractures treated with syndesmotic screws, open fractures, neurodegenerative diseases, chronic low back pain, previous spinal surgery, psychiatric disorders, alcoholism, drug addiction, body mass index greater than 30 and any associated fractures or orthopedic conditions limiting independent ambulation. This approach ensures a relatively homogeneous cohort, consistent with others fracture rehabilitation research (Haralson et al., 2025; Bretherton et al., 2024).

Participants are categorized into four groups according to the site of fracture and the postoperative loading protocol: Early Weight-Bearing (EWB) for ankle fractures (EWB ANKLE), Restricted Weight-Bearing (RWB) for ankle fractures (RWB ANKLE), EWB for tibial plateau fractures (EWB TIBIA) and RWB for tibial plateau fractures (RWB TIBIA). The allocation to postoperative rehabilitation protocols is determined independently by the operating surgeons prior to patient enrollment, based on fracture characteristics, intraoperative findings, patient comorbidities and clinical judgment. Randomization is not employed in order

to preserve individualized clinical decision-making, consistent with the observational design of the study.

Postoperative rehabilitation protocols are tailored according to fracture stability. For ankle fractures (EWB ANKLE), partial weight-bearing of 20 kg is initiated immediately postoperatively, advancing to full weight-bearing by the third week (Haralson et al., 2025). Tibial plateau fracture patients commence brace-assisted partial loading in the first postoperative week, consistent with accelerated rehabilitation protocols (Williamson et al., 2018).

The RWB protocol for ankle fractures consists of cast immobilization with non-weight-bearing for approximately four weeks, followed by gradual load progression (Swart et al., 2015). For tibial plateau fractures, the RWB protocol involves immobilization with a splint or adjustable knee brace and the use of crutches.

All patients are prescribed twenty physical therapy sessions, conducted two to three times weekly at the Physiotherapy Bachelor Degree Program of the University of Trieste or affiliated public health services. Additional sessions are prescribed during follow-up visits based on clinical need. Rehabilitation commences approximately seven days post-surgery for the EWB groups or upon cast or brace removal for the RWB groups. Early rehabilitation goals focus on edema control, pain management and progressive mobilization (Nash et al., 2004). Gait training, weight-bearing re-education and functional recovery exercises are integrated accordingly, with similar protocols for RWB patients implemented with a temporal delay (Gashi et al., 2023; Arnold et al., 2017; Moseley et al., 2015; Marchioni et al., 2019).

Data collection occurs at three postoperative time points: six weeks, three months and six months. During clinical follow-ups, the operating surgeons' protocols are adhered to and any braces are removed for motion capture evaluations. Outcome measures encompass both objective and subjective domains. Objective measures include ground reaction forces recorded

during the motor tasks, with GRF parameters normalized to body mass and limb length. Symmetry indices between the operated and contralateral limbs are calculated to quantify functional recovery. Temporal gait variables such as step length and velocity are also extracted. Moreover, the trajectory of the center of mass relative to the center of pressure (COM-COP) is analyzed to assess postural control and dynamic stability. Clinical assessments include goniometric measurements of passive range of motion (ROM), performed by a physiotherapist using standardized long-brace goniometric techniques (see *General Methods* for specifics).

Subjective patient-reported outcome measures are region-specific and validated; the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is used for tibial plateau fractures (Bellamy et al., 1988), while the American Orthopaedic Foot and Ankle Society (AOFAS) score (Kitaoka et al., 1994) and the Olerud-Molander Ankle Score (OMAS) (Olerud & Molander, 1984) are employed for ankle fractures. Additional assessments involve the Numeric Rating Scale (NRS) for perceived pain (Jensen et al., 1986; Hjermstad et al., 2011) and the evaluation of functional independence in activities of daily living (ADLs). Information regarding the return to sports or recreational activities was also recorded when applicable.

As a monocentric study, the sample size is determined by feasibility constraints rather than formal power calculations, consistent with exploratory biomechanical research (Arnold et al., 2019).

Statistical analyses for between-groups comparisons employ non-parametric tests (Mann-Whitney U test and Fisher's exact test) are selected due to non-normal data distribution and small sample size and are conducted using Jamovi 2.3.18.0. A significance level of $p < 0.05$ is adopted.

No techniques are applied to estimate or replace missing follow-up data; analyses are conducted using all available data points to optimize the use of collected information. While this strategy maintains the integrity of the observed dataset and supports internal validity, it

may introduce attrition bias if the missing data are not completely random, which could affect the broader applicability of the results.

Ethical approval for the study was granted by the Regional Ethics Committee (CEUR – protocol 147_2020) on March 16, 2021 and the study adheres to the Declaration of Helsinki principles. All participants provide written informed consent after receiving detailed explanations of study procedures, potential risks and benefits. Data processing is conducted in compliance with the European Union General Data Protection Regulation (EU Regulation 2016/679, GDPR). Patient information is anonymized prior to analysis and securely stored on password-protected offline systems accessible solely to authorized researchers.

Despite adherence to methodological rigor, several potential sources of bias must be acknowledged due to the study's observational, non-randomized design. The decision to assign patients to early or restricted weight-bearing protocols was influenced by the operating surgeon's clinical judgment, which incorporated fracture characteristics and patient comorbidities. This non-random allocation may have introduced selection bias and confounding, as baseline differences in age, sex, body mass index, fracture complexity, occupational demands and pre-injury physical activity levels could have independently influenced rehabilitation outcomes and internal validity. Additionally, the absence of blinding among patients and assessors raises the possibility of measurement bias, as knowledge of assigned protocols may have affected the administration and interpretation of clinical tests and patient-reported outcomes. Patient-reported questionnaires, while validated, are inherently susceptible to recall bias given their retrospective nature and the repetitive or overlapping items might have contributed to reporting bias through misinterpretation or survey fatigue. Furthermore, variability in rehabilitation settings and providers, despite overall guideline adherence, may have introduced interventional heterogeneity and measurement inconsistencies. Differences in patient adherence, motivation and access to physiotherapy

services, which could not be strictly controlled, may also have affected recovery trajectories in a non-uniform manner.

3.2.3 Results

Data collection is complete for 48 patients who met the inclusion criteria and consented to participate in this prospective observational study. The cohort had a mean age of 42.09 years (SD 15.47) and included 22 females. Due to the timing of enrollment, not all patients completed all scheduled follow-ups.

Two patients withdrew from the study owing to unrelated medical conditions (one patient reported neurological issues and another patient developed a oncological condition), which were deemed unrelated to the fracture fixation procedures.

Patients are stratified into two rehabilitation groups: the Early Weight-Bearing (EWB) group, consisting of 26 patients (mean age 41.16, SD 16.56), subdivided into 14 ankle fracture cases (mean age 42.78, SD 17.03) and 12 tibial plateau fracture cases (mean age 41.18, SD 17.30); and the Restricted Weight-Bearing (RWB) group, comprising 20 patients (mean age 43.20, SD 14.39), including 15 ankle fractures (mean age 44.85, SD 14.24) and 5 tibial plateau fractures (mean age 36.6, SD 15.37). Demographic characteristics and fracture patterns are comparable between groups, with no statistically significant differences detected. Many patients reported engaging in sports regularly prior to injury. At the initial six-week evaluation, some patients continue to use braces or maintain weight-bearing restrictions but nonetheless complete self-assessment questionnaires.

Clinical and functional outcomes

No surgery- or fracture-related complications are reported in any patient throughout the study period.

At 6 weeks post-operation, patients undergoing tibial plateau fixation reported full independence in activities of daily living (ADL). Among those with ankle fractures, patients in the EWB group demonstrated a trend toward superior recovery compared to the RWB group. Tibial surgery patients (both EWB and RWB groups) reported ability to bear weight on the operated limb while standing (88% and 80% of patients reported being able to bear weight during normal activities), whereas ankle fracture patients under RWB scored significantly lower than those in the EWB group (Fisher’s exact test, $p = 0.05$).

By 3 months, all patients regain independence in ADL and weight-bearing capacity. While a greater proportion of EWB patients reported returning to work and sport activities at 6 weeks compared to RWB patients, these differences were not statistically significant and diminished over time, with the exception of a higher rate of return to sports among tibial fracture patients in the EWB group ($p = 0.04$ at 3 months).

Detailed outcomes are summarized in *Table 1*, highlighting clinical and functional measures including independence in ADL, weight-bearing balance, return to work and return to sport, assessed at 6 weeks, 3 months and 6 months post-surgery.

Table 1 - Clinical and functional outcomes. Significance for Fisher’s exact test.

	<i>EWB</i>	<i>RWB</i>	<i>*</i>	<i>EWB</i>	<i>RWB</i>	<i>*</i>
	<i>Ankle</i>	<i>Ankle</i>		<i>Tibia</i>	<i>Tibia</i>	
<i>Indipendence in ADL</i>						
- 6 weeks	83%	53%	0.21	100%	100%	
- 3 months	100%	100%		100%	100%	
- 6 months	100%	100%		100%	100%	
<i>Weight bearing balance</i>						
- 6 weeks	75%	33%	0.05*	88%	80%	
- 3 months	100%	100%		100%	100%	
- 6 months	100%	100%		100%	100%	

Return to work						
- 6 weeks	41%	33%	0.7	55%	2%	0.3
- 3 months	91%	86%	1.0	77%	100%	0.48
- 6 months	100%	100%		100%	100%	
Return to sport						
- 6 weeks	25%	6%	0.29	33%	0%	0.22
- 3 months	37%	33%	1.0	77%	16%	0.04*
- 6 months	66%	61%	1.0	88%	66%	0.45

Analysis of validated patient-reported questionnaires reveal no significant differences between groups over time in WOMAC scores for tibial fractures (*Table 2*) or AOFAS scores for ankle fractures (*Table 3*). The OMAS scores showed a significant improvement in the EWB ANKLE group at 6 weeks compared to RWB ANKLE group ($p = 0.047$ for U Mann-Whitney test), but differences at later time points were not significant (*Table 4*). Across all patient groups, clinically meaningful improvements exceeding 10 points were noted between baseline and subsequent assessments.

Table 2 - WOMAC mean scores for patients operated after tibial plateau fracture. An improvement greater than 10 points is considered significant for research. Significance for U Mann-Whitney test.

WOMAC	EWB	RWB	p-value
T1	31.44	23.66	0.31
T2	14.11	11.5	0.37

Table 3 - AOFAS mean scores for patients operated after ankle fracture. An improvement greater than 10 points is considered significant for research. Significance for U Mann-Whitney test.

AOFAS	EWB	RWB	p-value
T1	71.50	64.93	0.242
T2	75.33	84.65	0.218
T3	86.67	91.07	0.40

Table 4 - OMAS mean scores for patients operated after ankle fracture. An improvement greater than 10 points is considered significant for research. Significance for U Mann-Whitney test.

OMAS	EWB	RWB	p-value
T1	61.25	40.66	0.047*
T2	69.44	67.50	0.82
T3	85	86.15	0.56

The values presented in *Figure 8* and *Figure 9* represent the mean total range of motion (ROM) data, calculated as the sum of flexion and extension degrees for each study group. Both tibial plateau and ankle fracture patients showed progressive improvement over time. Some missing data for EWB TIBIA patients at 6 months (T3) were due to timing of data acquisition. In the ankle surgery cohorts, mean total ROM measurements indicated superior joint mobility in the EWB group compared to the restricted weight-bearing (RWB) group.

Figure 8 - Range of motion mean values in patients operated after tibial plateu fracture. **Notes:** The values refer to the total ROM, calculated as the sum of the flexion and extension measurements. Due to acquisition timing, some EWB data are missing at T3.

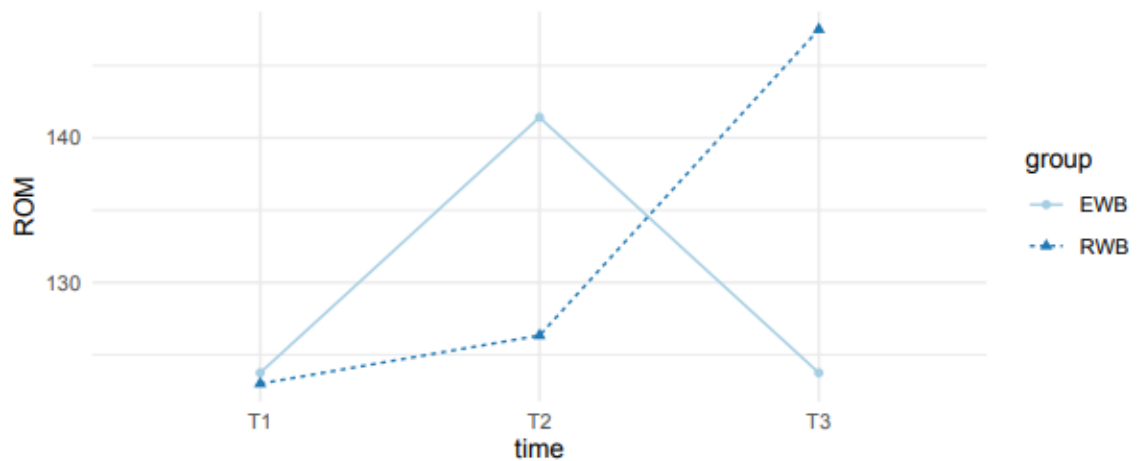
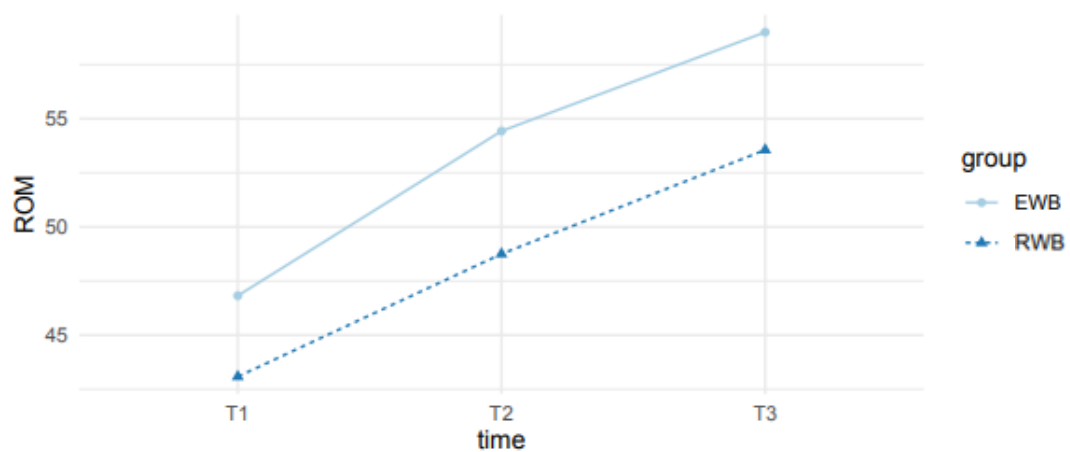


Figure 9 - Range of motion mean values in patients operated after ankle fracture. **Notes:** The values refer to the total ROM, calculated as the sum of the flexion and extension measurements.



The mean pain scores reported on the Numeric Rating Scale (NRS) are depicted in *Figure 10* and *Figure 11*. No group exhibited average pain levels exceeding 3.5 at any time point. Pain scores decreased progressively in all groups.

Figure 10 - NRS mean values for pain assessment in patients operated on after tibial plateau fracture.

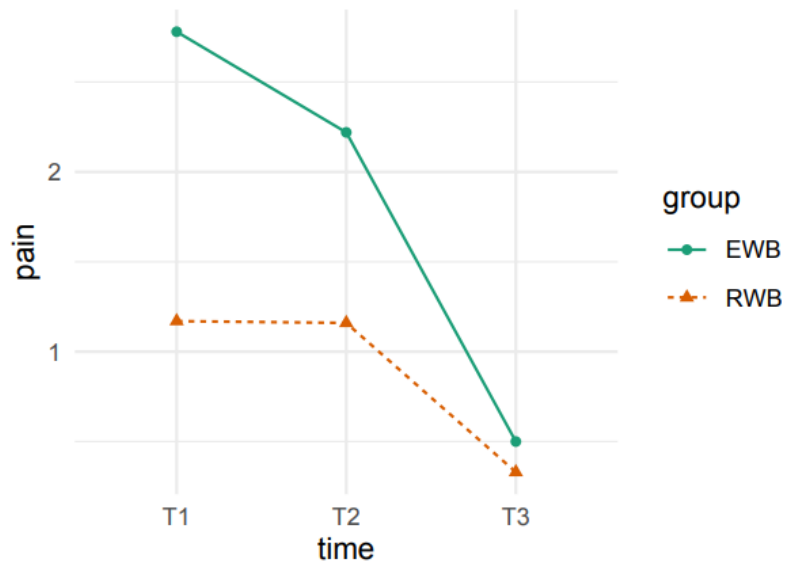
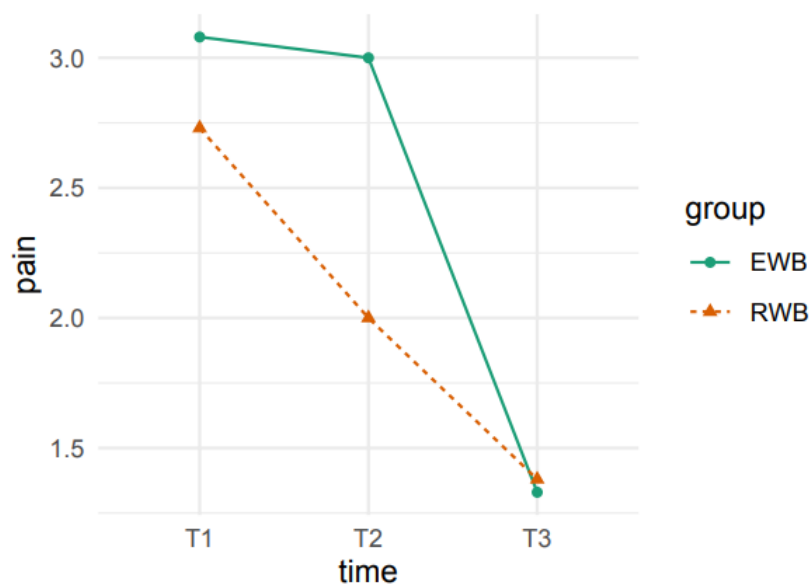


Figure 11 - NRS mean values for pain assessment in patients operated on after ankle fracture.



Gait analysis' data

Between-group comparisons of spatiotemporal gait parameters (step length, walking speed and symmetry) at 3 months post-surgery reveal no significant differences (Mann–Whitney U test, $p > 0.05$).

Data on the management of GRFs are compared at the 3-month evaluation, by which time all patients had regained full weight-bearing capacity and were already undergoing physiotherapy. Symmetry in the vertical GRF component ($f(z)$) is maintained across all groups during these tasks, indicating comparable balance functioning.

All groups maintain GRFs symmetry in the $f(z)$ component even during more dynamic tasks, such as sit-to-stand and gait initiation. The results of the GRFs analysis in $f(z)$ for patients operated on for tibial and ankle fractures, as shown in Table 5 and Table 6, reveal no significant differences between EWB and RWB groups within the same fracture category. These data will be discussed further below.

Table 5: EWB ANKLE vs RWB ANKLE group means and differences in the gait analysis and GRFs results at 3 months evaluation. Significance for U Mann Whitney test.

ANKLE	EWB (mean)	RWB (mean)	Significance
<i>Walk</i>			
Step length	60.50	62.16	0.42
Step speed	0.87	0.98	0.95
Step time symmetry	49.45	50.45	0.79
f(z) symmetry	49.49	49.42	0.90
f(z) variability	43.17	35.93	0.21
min com-cop diff symmetry	46.49	52.11	0.96

f(x) symmetry	60.52	52.15	0.50
f(y) symmetry	50.86	47.89	0.60
<i>Static Eyes Open</i>			
f(z) symmetry	49.34	49.46	0.89
f(x) symmetry	53.07	50.04	0.74
min com-cop diff symmetry	52.28	49.21	0.81
<i>Static Eyes Closed</i>			
f(z) symmetry	49.73	49.50	0.89
f(x) symmetry	53.40	49.65	0.63
min com-cop diff symmetry	52.26	48.09	0.71
<i>Static Eyes Open and Arm Abducted</i>			
f(z) symmetry	49.71	52.10	0.34
f(x) symmetry	52.43	50.41	0.85
min com-cop diff symmetry	48.77	48.49	0.36
<i>Static Eyes Closed and Arm Abducted</i>			
f(z) symmetry	50.15	52.19	0.79
f(x) symmetry	52.83	47.45	0.70
min com-cop diff symmetry	51.71	48.56	0.39
<i>Sit-to-stand</i>			
f(z) peak symmetry	49.42	49.53	0.86
f(z) standing symmetry	48.60	50.08	0.81
f(x) peak symmetry	51.32	51.01	0.63
f(x) standing symmetry	51.78	51.71	0.37
min com-cop diff symmetry	52.90	48.40	0.83

<i>Rise-to-walk</i>			
f(x) symmetry	63.79	62.23	0.76
min com-cop diff symmetry	49.72	47.11	0.84
<i>Gait Initiation</i>			
f(z) symmetry	48.87	49.01	0.77
f(x) symmetry	47.86	44.40	0.54
f(y) symmetry	51.51	52.54	0.69
min com-cop diff symmetry	54.85	48.73	0.77

Table 6: EWB TIBIA vs RWB TIBIA group means and differences in the gait analysis and GRFs results at 3 months evaluation. Significance for U Mann Whitney test.

TIBIA	EWB (mean)	RWB (mean)	Significance
<i>Walk</i>			
Step length	66.85	66.66	0.91
Step speed	1.10	1.22	1
Step time symmetry	50.34	49.66	0.87
f(z) symmetry	47.27	48.80	0.77
f(z) variability	43.77	40.84	0.60
min com-cop diff symmetry	51.83	57.56	0.93
f(x) symmetry	54.75	49.79	0.37
f(y) symmetry	50.18	46.45	0.24
<i>Static Eyes Open</i>			
f(z) symmetry	50.27	50.12	0.45
f(x) symmetry	49.87	47.96	0.65

min com-cop diff symmetry	50.48	51.37	0.98
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Static Eyes Closed

f(z) symmetry	50.62	50.77	0.65
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f(x) symmetry	48.02	47.83	0.98
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min com-cop diff symmetry	48.98	49.86	0.74
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Static Eyes Open and Arm Abducted

f(z) symmetry	50.97	53.88	0.55
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f(x) symmetry	48.38	48.31	1
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min com-cop diff symmetry	51.12	51.34	0.56
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Static Eyes Closed and Arm Abducted

f(z) symmetry	52.58	54.20	0.50
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f(x) symmetry	47.29	47.59	0.75
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min com-cop diff symmetry	48.45	50.66	0.40
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Sit-to-stand

f(z) peak symmetry	47.98	45.63	0.71
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f(z) standing symmetry	50.30	51.17	1
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f(x) peak symmetry	49.60	50.93	0.98
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f(x) standing symmetry	49.90	53.56	0.105
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min com-cop diff symmetry	48.71	50.44	0.76
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Rise-to-walk

f(x) symmetry	59.73	53.88	0.52
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min com-cop diff symmetry	44.56	53.18	0.48
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Gait Initiation

f(z) symmetry	48.59	48.73	0.96
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f(x) symmetry	46.70	43.85	0.95
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f(y) symmetry	51.27	51.77	0.96
min com-cop diff symmetry	49.05	58.21	0.45

3.2.4 Discussion

This prospective observational study adds to the expanding literature supporting early weight-bearing (EWB) protocols for surgically treated lower limb fractures. Our results are in line with recent randomized controlled trials that have found no significant difference in complication rates between EWB and restricted weight-bearing (RWB) groups, both for ankle and tibial plateau fractures (Canton et al., 2022; Bretherton et al., 2024). Notably, no adverse events related to the surgical procedure or fracture site were observed in either group throughout the follow-up period. This supports the safety profile of EWB as a viable rehabilitation strategy, consistent with the study from Passias et al., which reported similar hardware failure rates between EWB and RWB protocols (Passias et al., 2020). However, the strict exclusion of high-risk patients in this study (e.g., smokers, diabetics) limits direct comparability to real-world populations, where comorbidities may elevate complication risks (Larsen and Elsoe, 2025).

Unlike some previous studies that implemented daily physiotherapy, our patients received two to three sessions per week, starting within the first week after surgery. This suggests that the timing of mobilization may be more critical than the sheer frequency of physiotherapy sessions in driving early functional recovery.

Functionally, patients in the EWB group demonstrated a trend toward more rapid recovery, particularly in independence in activities of daily living and return to work and sports at 6 weeks postoperatively. While these differences did not reach statistical significance in most comparisons, they represent clinically meaningful improvements, especially considering the

impact of early functional restoration on quality of life (Kubiak et al., 2013). The difference in the item related to return to sports is easily explained for RWB patients, where weight-bearing restrictions inevitably delayed the return to higher-intensity activities.

Among the patients monitored in this study, a clinically meaningful improvement was observed in the AOFAS, OMAS and WOMAC functional questionnaires, justifying the focus on the 3-month follow-up assessment (T2) for gait analysis. Across all groups, patients demonstrated clinically significant gains, defined as increases exceeding 10 points, within the first three months post-intervention. The early weight-bearing groups exhibited smaller improvements between the 6-week (T1) and 3-month (T2) evaluations, likely because they had already achieved scores more than 10 points higher than the restricted weight-bearing groups at the initial assessment. By the 6-month follow-up, functional outcomes converged further, indicating comparable recovery levels across groups. This overall positive trajectory is likely influenced by the relatively young age and active lifestyle of the study population.

Our non-significant trends in early functional scores may reflect insufficient power, but the clinically relevant improvements in ADL independence at 6 weeks (EWB: 68% vs. RWB: 52%) align with qualitative studies emphasizing patient prioritization of functional autonomy over radiographic outcomes (Trickett et al., 2012).

Data obtained through motion analysis enabled the assessment of differences between study groups in tasks resembling real-life movements. This approach, alongside administered questionnaires and clinical evaluations, allowed for a more analytical observation of the recovery level in these patients.

In this study, only 3-month follow-up results are presented, as at this follow-up all patients had already returned to a good functional level and were able to bear weight and use the operated limb in daily life activities.

Gait analysis provided suggestions into biomechanical recovery. Although no statistically significant differences were detected in spatiotemporal parameters between groups, patterns in ground reaction force (GRF) management suggest subtle biomechanical adaptations: EWB patients with ankle fractures (EWB ANKLE) exhibited a tendency toward greater lateral GRF shifts in the mediolateral GRF component ($f(x)$ component). Patients in the RWB ANKLE group tended to maintain a more medial load. Overall, these findings may support the results of the study by Wang et al. (2010) who conducted gait analysis in 18 individuals with ankle fractures (including lateral malleolar and trimalleolar fractures) twelve months post-surgery. They reported reduced gait speed, single support time and push-off duration on the operated side compared to the non-operated side. The authors suggested that these alterations may stem from a compensatory strategy in which patients lift the foot rather than generating propulsion, thereby prolonging the double support phase (Wang et al., 2010). In the present study, EWB ANKLE patients may have exhibited improved load acceptance and push-off dynamics compared to the RWB ANKLE group, suggesting more efficient weight transfer and propulsion patterns.

The lateral GRF shifts observed in EWB ankle patients are consistent with the findings of Mirando et al. (2022), who reported lateralization of load during gait following ankle fractures as part of biomechanical adaptations in the recovery process. This contrasts with the decreased between-steps trunk movement symmetry described by Hsu et al. (2018), suggesting that differences in rehabilitation protocols, particularly regarding weight-bearing progression, may influence distinct biomechanical recovery patterns.

In tibial plateau fractures, both groups favored a more medialized GRF distribution, likely reflecting cautious joint alignment management during knee rehabilitation. In the literature, more medialized ground reaction force distribution during gait, has been linked to a protective strategy to minimize lateral compartment loading (Kumar et al., 2014).

During static postural tasks, especially under dual-task conditions such as standing with eyes closed and upper limb abduction, patients in the early weight-bearing groups (EWB TIBIA and EWB ANKLE) demonstrated greater ability to maintain symmetry in the vertical ground reaction force ($f(z)$) component. This finding aligns with previous research indicating that early mobilization in the recovery after anterior cruciate ligament reconstruction facilitates more effective postural control and balance, even when additional motor demands are introduced (Grueva–Pancheva et al., 2023). In contrast, restricted weight-bearing patients (RWB TIBIA and RWB ANKLE) exhibited a tendency to disproportionately load the operated limb, reflecting a compensatory strategy that limits their capacity to adjust for imbalances induced by the concurrent task. Similar patterns have been observed in studies of weight-bearing asymmetry following lower limb surgery, where delayed or limited loading is associated with reduced postural adaptability and increased reliance on the affected side (De Leo et al., 2024). The influence of upper limb positioning on balance control has been shown to amplify postural demands, thereby exposing differences in neuromuscular strategies between patients with varying rehabilitation protocols (Degot et al., 2020). When visual input is removed, as in eyes-closed static standing, postural control becomes more reliant on vestibular and proprioceptive feedback (Peterka, 2002). This shift often results in decreased postural sway and challenges in maintaining symmetrical ground reaction forces. Early weight bearing could enhance the integration of somatosensory and vestibular inputs essential for maintaining balance in the absence of visual cues.

Although the relatively small sample size and strict inclusion criteria limited the statistical power and generalizability of our results, they likely minimized confounding factors associated with prolonged disability.

In both restricted weight-bearing (RWB) patient groups, a lower, although not statistically significant, variability in the vertical ground reaction force ($f(z)$) component was

observed, measured as the difference between the highest and lowest peaks during the stance phase of gait. This asymmetry may indicate a more cautious gait pattern with limited dynamic adjustments.

The reduced $f(z)$ variability did not achieve symmetry relative to the contralateral limb, even in early weight-bearing (EWB) groups but may reflect greater confidence in the operated limb across different phases of the gait cycle, as well as an enhanced capacity to adapt to load transfer and acceptance during walking for the EWB groups.

Biomechanically, variability in GRF during stance phases is fundamental to dynamic stability and the ability to respond to perturbations, as described in foundational analyses of gait mechanics (White et al., 1999). The higher variability seen in EWB patients likely reflects an improved neuromuscular capacity to modulate forces dynamically, supporting more effective postural control and functional recovery. In contrast, the lower variability in RWB patients may signify a protective strategy that prioritizes stability over adaptability, potentially limiting long-term functional gains.

The lateral shift of GRFs in the $f(x)$ component is not observed in patients who underwent surgery for tibial plateau fractures in either of the two groups studied. Both the EWB TIBIA and RWB TIBIA groups show a greater tendency to maintain these $f(x)$ forces more inward, likely because greater emphasis is placed on joint alignment during recovery from knee fractures.

During the analyzed task of gait initiation, all patient groups exhibited a greater tendency to maintain GRFs in the $f(x)$ component more externally on the contralateral limb to the operated one. Considering that the first step was taken with the operated limb and that a lateral shift of GRFs in the $f(x)$ component was observed during the postural adjustment preceding the initiation of gait on the unaffected limb, this increased lateral shift during the

imbalance phase could be interpreted as an altered swing preparation strategy for the operated limb for the first step, along with heightened attention to the movement execution. In both types of fractures, RWB patients exhibited this deviation of GRFs toward the $f(x)$ direction more prominently, although without reaching statistically significant differences compared to the other EWB groups.

During gait, both EWB groups show a greater tendency to laterally shift the GRFs in the $f(x)$ component during the loading phase on the operated limb; however, both RWB groups demonstrate lower symmetry in the anteroposterior direction of GRFs in the $f(y)$ component, which can be attributed to increased dependency of the intact limb during gait, as reported by Raza (Raza et al., 2024). The reduction in anteroposterior displacement relative to the contralateral limb in the observed patients, however, contrary to what was reported in a previous study (Iliopoulos et al., 2020), does not correspond to a reduction in the single operated limb's stance time, which can be ascribed to a load avoidance behavior.

Due to the observational nature of the present study, several potential sources of bias must be acknowledged. First, although participants are stratified according to the anatomical site of fracture and weight-bearing protocol, there are variations in fracture complexity. These differences could influence both the clinical decision-making process and the trajectory of post-operative recovery. Additionally, patients' occupational demands and their pre-injury levels of physical activity were not systematically recorded. These factors may have affected both the ability and motivation to engage in rehabilitation, as well as overall functional outcomes. While the inclusion criteria aimed to minimize variability by restricting the sample to individuals aged between 18 and 65 and with a body mass index (BMI) below 30, demographic heterogeneity remained. Factors such as age, sex and BMI (even within the accepted ranges) are known to influence healing rates, rehabilitation responses and long-term outcomes. Study participants

were predominantly employed adults with high baseline activity levels, whereas outcomes may differ in sedentary populations less motivated for early mobilization (Al-Hourani et al., 2024).

However, it is important to recognize that the exclusion of patients with multiple comorbidities, such as diabetes or obesity, may limit the generalizability of our results to higher-risk populations, where neuromuscular inhibition and delayed healing are more prevalent (Gupta et al., 2023). Excluding polytrauma and osteoporotic fractures limits applicability to geriatric populations, where fracture patterns and healing capacity differ substantially.

The biomechanical findings' generalizability is further complicated by emerging evidence of regional variability in gait patterns. For example, the observed lateral GRF shifts conflict with data from Asian cohorts showing predominantly medial load redistribution post-ankle fracture (Chen et al., 2024), possibly reflecting anthropometric or cultural differences in movement strategies.

Another important consideration is the lack of randomization. The decision to assign patients to early or restricted weight-bearing protocols was made independently by the operating surgeon, prior to study enrollment, based on clinical judgment and fracture characteristics. This may have introduced selection bias or confounding by indication, as patients with more stable fractures or fewer comorbidities may have been preferentially assigned to early mobilization. Moreover, while all patients followed a structured rehabilitation program, therapy was delivered by different clinicians and potentially with variable adherence, which could introduce performance bias. Finally, the use of self-administered outcome questionnaires introduces the possibility of recalling or reporting bias, as patients' perceptions of pain, function and quality of life are inherently subjective and may be influenced by expectations or emotional state at the time of assessment.

Although efforts were made to standardize evaluations and treatment protocols, these inherent limitations underscore the complexity of conducting observational clinical research in surgical populations and highlight the need to interpret the findings with appropriate caution.

The absence of significant observable alterations through motion analysis in the present study may be attributable to the small sample size examined, as well as to the recruitment methodology, which in other studies did not include such stringent exclusion criteria. The intention to reduce the number of variables that could influence the results limited the ability to achieve a larger sample size during the study period. Likely, the strict inclusion criteria, which also contributed to the low sample size, have minimized or eliminated the effects of other factors that contribute to prolonged disability, as reported by the majority of literature articles, which do not typically specify such rigid inclusion/exclusion criteria.

Although this study does not highlight a difference between the observed groups in gait analysis results, it aligns with the literature supporting theories that suggest that, despite the immediate consequences of inactivity/immobilization extending to the cortical level, a return to activity allows patients to reverse these processes and achieve comparable results between the two groups. In fact, the decision to assess patients at 6 weeks, 3 months and 6 months allowed for the evaluation of all patients following an initial rehabilitation period, rather than immediately after the removal of the cast or at the time of weight-bearing allowance, as was done in other studies in the literature.

This study does not include the number of physiotherapy sessions performed as an outcome measure, nor the overall costs to the national health system. However, in many accredited private rehabilitation centers, therapies are provided on a daily basis. Therefore, the prolongation of sessions in cases of delayed weight-bearing and the subsequent need to recover altered capacities undoubtedly represent a higher expense for the healthcare system. Although

not quantified here, the trend toward faster functional recovery in EWB patients aligns with cost-utility models predicting lower rehabilitation costs compared to RWB (Bretherton et al., 2024). This economic advantage likely stems from reduced physiotherapy duration and earlier return to productivity, factors increasingly prioritized in value-based care frameworks.

Despite the limitations of evaluating within a laboratory setting rather than in an ecological context, this study proposed a thorough analysis of the management strategies of ground reaction forces in patients who underwent surgery for lower limb fractures, both with and without early weight-bearing allowance. These findings could highlight important considerations in the design of physiotherapy pathways for patients with similar fractures.

This study supports the safety and potential functional benefits of early weight-bearing after surgical fixation of lower limb fractures with moderate rehabilitation frequency (2–3 sessions/week), to mitigate movement alterations after ankle and tibial plateau fractures while maintaining surgical safety. The clinical, functional and biomechanical data provide valuable insights into how early loading influences long-term functional adaptation, supporting the rationale for reconsidering weight-bearing restrictions and tailoring rehabilitation protocols to optimize patient outcomes. Future randomized trials should focus on validating these laboratory-based findings to confirm the results and refine the postoperative management, also with wearable sensor technology.

Together, these studies underscore the importance of early weight-bearing in promoting not only confidence and stability in the operated limb but also the dynamic adaptability necessary for efficient load transfer during gait. They also highlight that while early mobilization improves certain biomechanical parameters, complete restoration of symmetry and variability patterns remains a challenge in post-fracture rehabilitation.

3.3 Study 2. Early rehabilitative treatment for patients with partial weight-bearing restrictions using antigravity treadmill with non-immersive virtual reality: an observational study

Abstract

Patients undergoing surgical fixation for lower limb fractures often face weight-bearing restrictions during early rehabilitation, which can hinder recovery by causing muscle atrophy, joint stiffness and impaired neuromuscular control. Early mobilization is critical to preventing these complications and to preserving central motor patterns essential for functional recovery. Anti-gravity treadmills have recently emerged as a promising alternative, enabling progressive weight-bearing with minimal joint stress. Functional and biomechanical effects of this approach remain underexplored. This prospective monocentric cohort study aims to address this gap by employing objective gait analysis and functional assessments to evaluate the use of an anti-gravity treadmill combined with non-immersive virtual reality for rehabilitation following complex lower limb fractures. Clinical, functional and biomechanical outcomes of a rehabilitation protocol incorporating anti-gravity treadmill therapy with non-immersive virtual reality will be compared to a historical cohort of patients with early weight-bearing allowed after surgery.

Patients undergoing internal fixation for distal femur, proximal tibia or tibial pilon fractures participated in the program including treadmill sessions and physiotherapy. Clinical, patient-reported and biomechanical outcomes were assessed at 6 weeks, 3 months and 6 months post-surgery and compared with the early weight-bearing (EWB) cohort. All treadmill patients regained independence in daily activities by 3 months, with satisfactory pain control, joint mobility and functional scores. Gait analysis revealed effective load management despite observed asymmetries in ground reaction forces. Compared to the EWB group, treadmill

patients returned to work earlier after tibial plateau fractures. No significant differences were found in WOMAC scores. Although promising, findings are exploratory due to the observational design and require confirmation through randomized controlled trials.

3.3.1 Introduction

Patients undergoing surgical fixation for lower limb joint fractures, particularly involving the ankle or tibial plateau, are frequently prescribed partial or complete weight-bearing restrictions during the early postoperative period. This phase, which can last up to 12 weeks, requires careful clinical judgment to determine whether weight-bearing should be allowed and, if so, the appropriate extent to minimize the risk of compromising fracture healing (Stinner et al., 2022; van der Vusse et al., 2017). However, adherence to prescribed weight-bearing limits is often difficult for patients, due to pain, balance deficits, or lack of proprioceptive feedback, which may result in unintentional overloading or underloading of the affected limb. Such challenges can negatively impact rehabilitation adherence and ultimately functional outcomes (Hustedt et al., 2012).

The consequences of restricted loading extend beyond the fracture site, as prolonged immobilization or limited weight-bearing can lead to muscle atrophy, disuse-induced tissue degeneration, joint stiffness and impaired proprioception, all of which contribute to delayed recovery and reduced functional capacity (Leung et al., 2015; Jan et al., 2009). Muscle atrophy, in particular, has been shown to occur rapidly during periods of unloading, with significant loss of muscle mass and strength observed within weeks (Gao et al., 2018; Wall et al., 2014), underscoring the importance of early interventions to preserve musculoskeletal integrity. Moreover, joint stiffness and decreased proprioceptive acuity can impair balance and gait, increasing the risk of falls and further injury (Raizah et al., 2023; Shen et al., 2024).

Beyond the musculoskeletal effects, early rehabilitation prevents maladaptive cortical reorganization that can occur following prolonged immobilization and restricted loading. Cortical adaptations may lead to altered motor control and impaired neuromuscular coordination, which can hinder functional recovery (Sharma et al., 2013; Liepert et al., 1995; Frotuna et al., 2013). Prolonged use of assistive devices and non-weight-bearing can lead to maladaptive movement strategies (Quested et al., 2017). Timely and targeted interventions are essential to preserve central motor patterns and ensure effective long-term functional recovery. Early mobilization approaches that incorporate safe, gradual weight-bearing (Smeeing et al., 2015) combined with physical therapy program (Eladl et al., 2025) have demonstrated effectiveness in enhancing muscle strength, joint mobility and proprioceptive function, balancing protection of the healing fracture with interventions that minimize the negative impact of unloading (Raza et al., 2024; Bade et al., 2011). Patient education and adherence are critical components: clear communication and supervised rehabilitation sessions have been shown to increase compliance and optimize functional gains (Fernandes et al., 2023).

Hydrotherapy, such as walking in water, has historically been employed to reduce load during rehabilitation, leveraging buoyancy to facilitate early mobilization (Fappiano et al., 2008). However, its use is often limited by logistical and infrastructural constraints, including availability and patient access (Rahman, 2024). In contrast, anti-gravity treadmills have emerged as a promising tool in orthopedic rehabilitation, enabling progressive reloading of the affected limb while minimizing stress on healing tissues (Trovato et al., 2024). This approach allows patients to gradually increase weight-bearing without compromising fracture stability or joint integrity, facilitating early mobilization and functional recovery (Trovato et al., 2024; Henkelmann et al., 2021; Hoyt et al., 2015). Patil et al. (2013) demonstrated that anti-gravity treadmills effectively reduce joint forces during gait, protecting postoperative tissues from overload while maintaining natural movement patterns. Similarly, Kim et al. (2020) reported

improved muscle strength and controlled weight-bearing progression in patients recovering from periarticular knee fractures using positive-pressure treadmill training. Liang et al. (2019) confirmed the safety and efficacy of anti-gravity treadmill, showing enhancements in gait parameters and muscle strength in orthopedic patients.

Helkelmann et al. (2021) found that anti-gravity treadmill reduced muscle atrophy and facilitates early mobilization and functional training after ankle and tibial plateau fractures. Compared to standard rehabilitation protocols, treadmill training allows for similar patient-reported outcomes at six weeks but results in significantly less muscle atrophy. Subsequent research conducted by Palke et al. (2022) reinforced the evidence of sustained benefits associated with treadmill-assisted rehabilitation, demonstrating improvements in dynamic gait function and preservation of muscle mass over the long term, all while maintaining comparable clinical outcomes to conventional rehabilitation methods. Other studies by Kim et al. (2020A; Kim et al., 2020B) have validated the safety and efficacy of positive-pressure treadmill training as an early weight-bearing intervention in orthopedic patients, reporting enhancements in muscle strength and normalized gait patterns, highlighting the potential of this modality to support functional recovery and facilitate a smoother transition to full weight-bearing activities.

Patil et al. (2013) provided additional evidence that anti-gravity treadmills effectively decrease the forces exerted on joints during walking. This reduction in joint loading helps to prevent excessive stress on healing tissues after surgery, thereby lowering the risk of postoperative complications related to overload. This unloading is achieved without disrupting the natural biomechanics of gait, allowing patients to maintain normal movement patterns while gradually increasing weight-bearing.

Others gait analysis studies in populations with cerebral palsy (El-Shamy et al., 2017; Lotfian et al., 2017), stroke (Oh et al., 2022) and knee osteoarthritis (Liang et al., 2019) have shown improved knee kinematics and joint loading, particularly during the loading response

phase, highlighting the device's potential to enhance neuromuscular control. Such biomechanical advantages make anti-gravity treadmills a valuable tool in early rehabilitation protocols aimed at optimizing recovery and neuromuscular control following lower limb fractures.

Cortical neuroimaging data reveal increased activation in motor-related brain regions during treadmill-assisted gait training, underscoring its neuroplastic potential (Ashtiyani et al., 2020). These findings suggest that avoiding prolonged non-weight-bearing may help maintain central motor patterns and accelerate recovery after orthopedic injuries.

Despite these advances, the functional and biomechanical impacts of anti-gravity treadmill training after lower limb fracture surgery remain insufficiently characterized, especially through gait analysis. While anti-gravity treadmills appear to offer a safe and effective rehabilitation tool, minimizing joint stress and muscle wasting, their role requires further investigation.

The current study aims to fill this gap using objective gait analysis and functional assessments to compare outcomes between patients undergoing rehabilitation with an anti-gravity treadmill combined with non-immersive virtual reality following complex lower limb fractures and a historical cohort of patients allowed early weight-bearing after surgery. Clinical, functional and biomechanical results from the rehabilitation protocol incorporating anti-gravity treadmill therapy with virtual reality will be evaluated against those from the early weight-bearing group to determine the effectiveness of this combined intervention.

Comparing anti-gravity treadmill training with early weight-bearing (EWB) protocols may clarify whether the benefits of treadmill use extend beyond load reduction to positively affect gait dynamics and motor control.

3.3.2 Materials and Methods

This prospective monocentric cohort study was conducted at the University of Trieste in collaboration with the Orthopedic and Traumatology Department of Cattinara Hospital (ASUGI), Trieste. The study enrolls patients who have undergone internal fixation for complex lower limb joint fractures, specifically distal femur fractures, proximal tibial fractures and C3-type tibial pilon fractures as classified by AO guidelines. Following surgical intervention, all patients are prescribed a touch-down weight-bearing protocol. Patients meeting the inclusion criteria are consecutively enrolled either during hospital admission, hospitalization, or outpatient follow-up at the same institution.

Rehabilitation activities, data collection and gait analyses are performed at the Physiotherapy Bachelor's Program of the University of Trieste. Biomechanical and clinical assessments take place in the Motion Analysis Laboratory equipped with eight high-speed infrared cameras and four centrally located force platforms calibrated prior to each session to ensure precise acquisition of kinematic and kinetic data. Patients are assessed barefoot along a 10-meter walkway, during which ground reaction forces (GRFs) were collected across various static and dynamic tasks designed to simulate daily activities, including standing under different visual (eyes open and eyes closed) and motor conditions, sit-to-stand, rise-to-walk, gait initiation and walking. Further methodological details concerning hardware, marker placement, data processing and theoretical frameworks are comprehensively described in the *General Methods* chapter.

Participants undergo a structured rehabilitation program consisting of 20 physiotherapy sessions spread over 10 weeks, with two sessions per week lasting 45 minutes each. Each session combines conventional physiotherapy with gait training on an anti-gravity treadmill augmented by non-immersive virtual reality. The treadmill is calibrated to provide body weight support through a thoracic harness system, featuring straps placed either beneath the groin or

around the proximal thighs, thus allowing patients to ambulate safely with diminished joint loading. The virtual environment, projected onto a 2D screen positioned in front of the treadmill, provides visual feedback intended to enhance gait mechanics without full immersion, maintaining therapist-patient communication and a familiar rehabilitation setting. Initial sessions employ a basic visual interface with rectangular step cues adjusted to individual stride lengths, facilitating assessment of step symmetry and familiarization with the equipment. Progressively, more complex visual scenarios simulating natural and urban landscapes are introduced to better approximate real-world walking conditions and redirect patients' attention away from the operated limb. The duration of treadmill use is gradually increased from approximately five minutes during the first session to up to twenty minutes per session as tolerated, with clinical staff monitoring patients for any physical or emotional discomfort related to the sensation of weight suspension. This approach ensures consistency across participants while allowing tailored progression, fostering safe motor learning and minimizing joint overload during early recovery.

To evaluate the effectiveness of this combined anti-gravity treadmill and virtual reality rehabilitation protocol, outcomes are compared with data from a previous cohort subjected to an early weight-bearing (EWB) protocol. The EWB cohort, who were permitted to bear weight after surgery, previously demonstrated the most favorable functional recovery in earlier analyses. This comparative approach aims to contextualize the effects of the novel multimodal intervention against an established, effective rehabilitation strategy.

Four groups are established based on the fracture location and the postoperative weight-bearing protocol: patients with ankle fractures undergoing treadmill training combined with non-immersive virtual reality (Treadmill ANKLE), those with ankle fractures following an early weight-bearing protocol (EWB ANKLE), patients with tibial plateau fractures receiving

treadmill training with non-immersive virtual reality (Treadmill TIBIA) and those with tibial plateau fractures managed with early weight-bearing (EWB TIBIA).

Follow-up assessments are conducted at three post-operative timepoints: six weeks, three months and six months. These evaluations include clinical examinations and gait analyses, enabling longitudinal monitoring of motor recovery and functional outcomes. Objective data collection focuses on GRFs during the specified motor tasks, with measurements normalized to body mass and limb length. Symmetry indices comparing the operated and contralateral limbs are calculated to quantify functional recovery. Additionally, temporal gait parameters such as step length and walking velocity are extracted and the trajectory of the center of mass relative to the center of pressure (COM-COP) is analyzed as an indicator of postural control and dynamic stability.

Alongside biomechanical metrics, clinical and patient-reported outcome measures are systematically collected. Functional status of the affected limb is assessed with validated, region-specific instruments: the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Index for knee involvement (Bellamy et al., 1988) and the American Orthopaedic Foot & Ankle Society (AOFAS) (Kitaoka et al., 1994) and Olerud-Molander Ankle Score (OMAS) scores for ankle fractures (Olerud&Molander, 1984). These assessments are conducted following a standardized schedule at six weeks, three months and six months postoperatively. Complementary clinical examinations include goniometric measurements of passive range of motion (ROM) carried out by a physiotherapist using a long-arm goniometer and standardized procedures. This method is recognized for its high inter-rater reliability when performed by experienced clinicians (Hancock et al., 2018). Evaluations of weight-bearing symmetry are performed using force plate in the motion analysis laboratory, providing objective data on load distribution and balance. Pain intensity is also assessed using the Numeric Rating Scale (NRS) (Hjermstad et al., 2011; Jensen et al., 1986), a validated and

reliable measure widely employed in orthopedic rehabilitation to monitor patient discomfort and guide pain management. The assessment includes evaluation of patients' functional independence in performing activities of daily living (ADLs) and return to sports or recreational activities is documented where applicable. The reliability and validity of these instruments are well-established in the literature and are presented in the *General Methods* chapter of this dissertation.

Data analysis is conducted using Jamovi software (version 2.3.18.0). Statistical comparisons between groups are performed using the Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables, with significance defined as $p < 0.05$. No methods are applied to handle missing data: all available data were used as observed without imputation or adjustment. This analysis ensures that results are based solely on actual measurements but introduces a bias: this approach may affect the generalizability of the findings, as systematic differences between cases with and without missing data could influence the study outcomes.

Others potential sources of bias inherent to the observational, non-randomized study design must be acknowledged. Allocation of patients to the rehabilitation protocol incorporating anti-gravity treadmill and virtual reality versus the historical EWB cohort was not randomized but based on clinical judgment and patient eligibility, potentially introducing selection bias. This decision process was influenced by fracture characteristics, surgical outcomes, patient comorbidities and overall clinical condition, which may confound observed differences in recovery trajectories. The absence of blinding for both patients and assessors poses a risk of measurement bias. Awareness of group assignment could have affected the administration or interpretation of clinical tests and patient-reported outcomes. Self-reported questionnaires such as the AOFAS, OMAS and WOMAC, while validated, are susceptible to recall bias as patients retrospectively evaluate their symptoms and function over preceding

weeks or months. The repetitive and overlapping nature of questionnaire items could have increased the likelihood of reporting bias caused by misunderstanding or participant fatigue during the survey. Variability in rehabilitation settings, therapists and patient adherence may have contributed to heterogeneity in treatment delivery and recovery outcomes. Differences in motivation, access to physiotherapy and individual engagement with the intervention could not be strictly controlled, potentially impacting results.

The study adhered to the Declaration of Helsinki and the European Union's General Data Protection Regulation (GDPR, Regulation 2016/679). Patient data were anonymized prior to analysis and securely stored on password-protected, offline systems accessible only to authorized personnel. Written informed consent was obtained from all participants after comprehensive explanation of study procedures, risks and benefits.

3.3.3 Results

A total of 20 patients met the inclusion criteria and agreed to participate in the study. The mean age of the overall cohort was 49.25 years (SD \pm 16.52), with nine female participants. The study population (Treadmill group) was divided into two subgroups based on the location of the fracture. The subgroup with malleolar fractures (Treadmill ANKLE) comprised 12 patients, with a mean age of 47.75 years (SD \pm 17.98), while the group with tibial plateau fractures (Treadmill TIBIA) included 8 patients, whose mean age was 51.5 years (SD \pm 14.93). Many participants reported engaging in regular sports or physical activities prior to their injuries.

At the time of the first assessment, conducted at six weeks postoperatively, several patients were still wearing a brace or had not yet achieved full weight-bearing on the operated

limb. Despite these limitations, all participants were able to complete the self-assessment questionnaires.

The clinical outcomes of the study group, who underwent rehabilitation incorporating an anti-gravity treadmill and non-immersive virtual reality, were compared with those of a previously studied cohort (EWB ANKLE and EWB TIBIA groups). These reference groups had been allowed to begin weight-bearing shortly after surgery and had shown the most favorable outcomes in the earlier study. No significant differences were observed in age or other demographic variables between the two cohorts. The Treadmill group sustained more complex fractures, for which the attending surgeons recommended more restrictive weight-bearing protocols during the initial postoperative phase.

Clinical and functional outcomes

The data reported by the patients are presented in Table 7 and Table 8. The data from the EWB group are re-presented for comparison between the two groups (Significance for Fisher's exact test).

No medical complications related to the surgical procedure or fracture site were reported in any of the cases in the Treadmill group. At six weeks post-surgery, all patients (100%) in the Treadmill group who had undergone tibial plateau fracture repair and 83% of those who had sustained ankle fractures reported being independent in their activities of daily living (ADLs).

By three months, all patients reported being confident in their ability to evenly distribute weight across both lower limbs. Notably, 87% of patients in the tibial plateau subgroup had

returned to work by the three-month evaluation, surpassing the return-to-work rate observed in the corresponding EWB subgroup (EWB TIBIA) (77%).

The full clinical and functional outcomes, including comparisons between the two groups, are summarized in *Table 7*. Patients in the Treadmill group demonstrated comparable or improved recovery in several domains, particularly among those who had undergone tibial surgery (Treadmill TIBIA).

Table 7 - Clinical and functional outcomes in Treadmill Groups compared to EWB groups.

	<i>Ankle</i>		<i>Tibial plateau</i>	
	Treadmill	EWB	Treadmill	EWB
<i>Independence in ADL</i>				
- 6 weeks	100%	83%	87%	100%
- 3 months	100%	100%	100%	100%
- 6 months	100%	100%	100%	100%
<i>Weight bearing balance</i>				
- 6 weeks	41%	75%	12.5%	88%
- 3 months	100%	100%	100%	100%
- 6 months	100%	100%	100%	100%
<i>Return to work</i>				
- 6 weeks	0.08%	41%	37.5%	55%
- 3 months	41%	91%	87%	77%
- 6 months	91%	100%	100%	100%
<i>Return to sport</i>				
- 6 weeks	0%	25%	0%	33%
- 3 months	25%	37%	12.5%	77%
- 6 months	42%	66%	62.5%	88%

Functional scores and pain scores also improved significantly over time. In the subgroup of patients with tibial plateau fractures, mean scores on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) decreased from 18.50 at six weeks to

11.85 at six months, indicating a clinically relevant improvement of more than 10 points. The literature reports an improvement of more than 10 points (observed in the Treadmill group already at the 3-month evaluation) as the minimal clinically important difference, allowing patients to walk without the need for assistive devices (Bretherton et al., 2024; Penning et al., 2023).

Comparative data for the EWB group were available only up to three months (mean WOMAC: 14.11), precluding direct comparison at six months (*Table 8*).

Table 8 - WOMAC mean scores for patients operated after tibial plateau fracture in Treadmill TIBIA group and EWB TIBIA group. An improvement greater than 10 points is considered significant for research.

<i>WOMAC</i>	Treadmill	EWB
T1	18.50	31.44
T2	18.85	14.11
T3	11.85	n/a

Functional outcomes measured by the American Orthopaedic Foot & Ankle Society (AOFAS) score for patients with ankle fractures improved steadily throughout follow-up. The mean score rose from 66.75 at baseline to 76.83 at three months and further to 86.34 at six months. These gains exceeded the minimal clinically important difference of 10 points reported in the literature and were comparable to the scores observed in the EWB group (*Table 9*).

Table 9 - AOFAS mean scores for patients operated after ankle fracture in Treadmill ANKLE group and EWB ANKLE group. An improvement greater than 10 points is considered significant for research.

<i>AOFAS</i>	Treadmill	EWB
T1	66.75	71.50
T2	76.83	75.33
T3	86.34	86.67

The evolution of joint mobility was monitored through measurements of the total range of motion (ROM), calculated as the sum of flexion and extension values and is illustrated in *Figure 12* and *Figure 13*. These figures refer to patients who underwent surgery for tibial plateau fractures and ankle fractures, respectively.

In the Treadmill TIBIA group (*Figure 12*), a progressive and clinically meaningful improvement in ROM was observed throughout the follow-up period. At the 6-week assessment, several patients still had movement restrictions, due to the use of bracing. By the 3-month evaluation, most patients demonstrated marked increases in joint excursion and by 6 months, ROM values approached or exceeded functional thresholds compatible with activities of daily living and return to work.

Patients in the Treadmill ANKLE group (*Figure 13*) exhibited a gradual restoration of ROM. Initial limitations at 6 weeks were expected given the nature of immobilization and restricted loading protocols typically associated with ankle injuries. From 3 to 6 months, there was a substantial increase in ROM, reflecting the transition to full weight-bearing and the more intensive physical rehabilitation. While inter-individual variability remained, the average ROM values at 6 months suggest that most patients regained a functional range of movement compatible with independent ambulation and basic recreational activity.

Figure 12 – Range of motion mean values in patient operated after tibial plateau fracture (Treadmill TIBIA and EWB TIBIA). **Notes:** The values refer to the total ROM, calculated as the sum of the flexion and extension measurements.

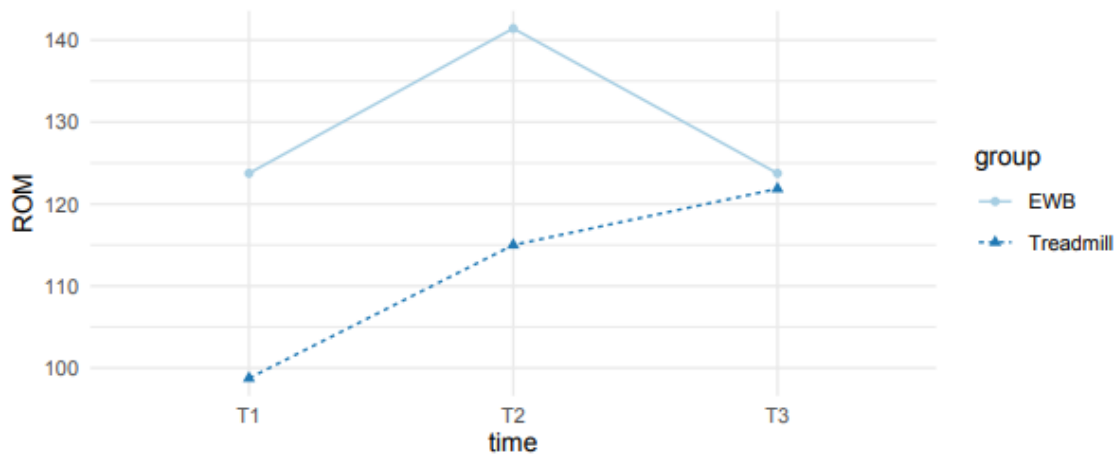
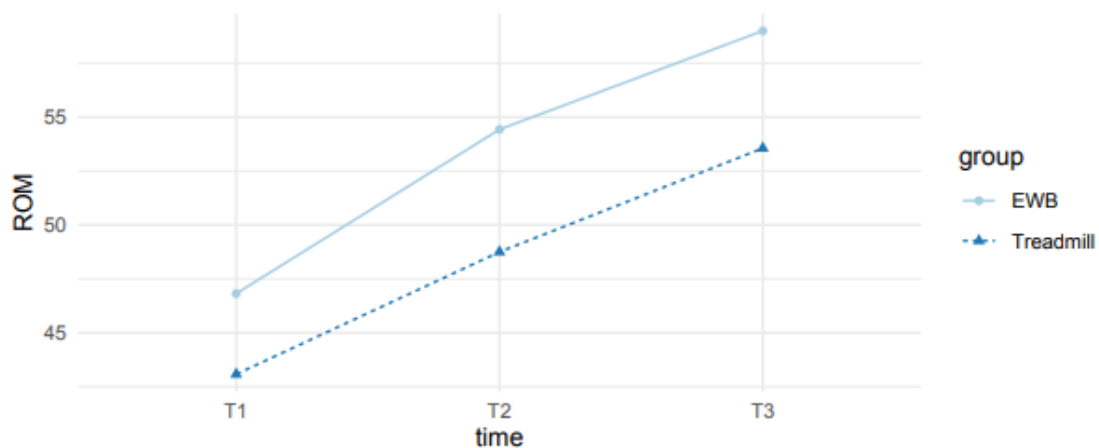


Figure 13 – Range of motion mean values in patient operated after ankle fracture (Treadmill ANKLE and EWB ANKLE). **Notes:** The values refer to the total ROM, calculated as the sum of the flexion and extension measurements.



Pain levels were monitored using the Numeric Rating Scale (NRS) at each follow-up interval and the results are presented in *Figures 14* and *Figure 15* for patients with tibial plateau

and ankle fractures, respectively. In both subgroups, a consistent reduction in perceived pain was observed over time.

In patients who underwent surgery for tibial plateau fractures (Treadmill TIBIA) (Figure 14), the average NRS pain score decreased substantially from the 6-week to the 6-month evaluation. While a slight increase in pain was reported by two individuals at the 3-month follow-up, possibly reflecting increased physical activity or changes in loading patterns, this trend was not sustained. By the 6-month mark, pain levels had decreased.

In the ankle fracture subgroup (Treadmill ANKLE) (Figure 15) pain scores were higher at the initial 6-week evaluation but progressively declined over time. By the 6-month follow-up, most patients reported minimal or no pain during weight-bearing and daily activities.

Figure 14 – NRS mean values for pain assessment in patients operated on after tibial plateau fracture (Treadmill TIBIA and EWB TIBIA).

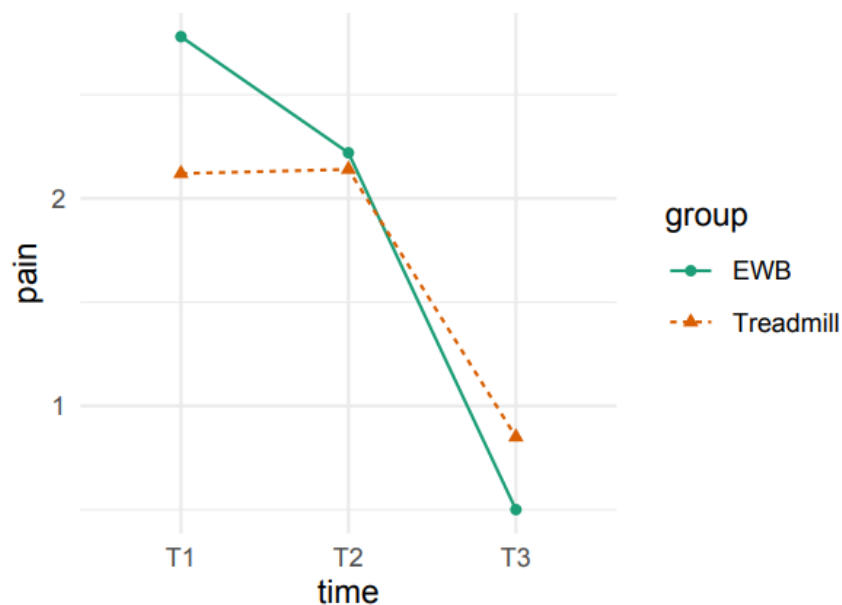
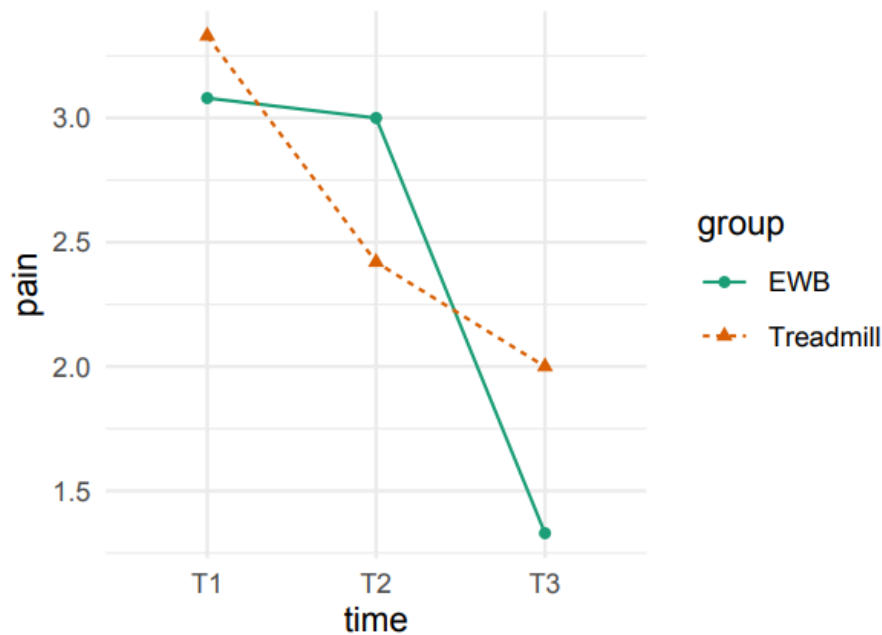


Figure 15 – NRS mean values for pain assessment in patients operated on after ankle fracture (Treadmill ANKLE and EWB ANKLE).



Gait analysis' data

Gait analysis' data are presented for the 3-month follow-up, a clinically relevant time point when patients typically transition to full weight-bearing and resume routine daily activities. This timing minimizes the confounding effects of early post-operative limitations and allows for a more valid assessment of functional recovery.

The analysis focused on comparing the operated and contralateral limbs across various gait and balance tasks, including walking, transitional movements and static balance tests, with spatiotemporal variables and ground reaction force (GRF) symmetry.

Spatiotemporal gait parameters (step length, velocity and stance time symmetry) did not significantly differ between the Treadmill and EWB groups. In the tibial plateau subgroup, patients in the Treadmill TIBIA group displayed slightly better symmetry in step time and step

length compared to the EWB TIBIA group. Although these differences did not reach statistical significance, they may indicate a more balanced gait pattern in the Treadmill TIBIA cohort.

Ground reaction force (GRF) data were normalized to each patient's limb length using Visual3D software. The GRF data offer additional insight into load distribution patterns. Detailed results of the gait analysis for both the tibial and ankle subgroups are presented in *Table 10* and *Table 11*. In patients with ankle fractures, the Treadmill ANKLE group demonstrated comparable or even slightly improved symmetry in vertical force application ($f(z)$) relative to the EWB ANKLE group across several tasks, including walking and dynamic transitions. In contrast, the mediolateral force patterns ($f(x)$) in the Treadmill group were shifted medially, whereas EWB patients displayed a more lateralized profile. Nonetheless, these differences did not reach statistical significance

When examining postural control tasks, such as static balance with and without visual input or abducted arm stance conditions, no significant group differences were detected between the subgroups in most parameters. However, in the ankle subgroup, a statistically significant difference emerged for $f(x)$ symmetry during eyes-closed static balance, with the EWB ANKLE group exhibiting higher lateral shift ($p = .042$) compared to Treadmill ANKLE group.

In tasks involving functional transitions, such as sit-to-stand, rise-to-walk and gait initiation, both groups demonstrated comparable performance with no significant differences in GRF symmetry.

Table 10 - Patients operated on for tibial plateau fractures: Treadmill TIBIA vs EWB TIBIA group means and differences in the gait analysis and GRFs results at 3 months evaluation. Significance for U Mann-Whitney test.

TIBIA	Treadmill (mean)	EWB (mean)	Significance
<i>Walk</i>			
Step length	52.00	66.85	0.41
Step speed	0.78	1.10	0.36
Step time symmetry	46.89	50.34	0.55
f(z) symmetry	48.90	47.27	0.81
f(z) variability	41.70	43.77	0.98
min com-cop diff symmetry	56.47	48.07	0.90
<i>Static Eyes Open</i>			
f(z) symmetry	46.46	50.27	0.56
f(x) symmetry	49.34	49.87	0.47
min com-cop diff symmetry	54.45	50.48	0.61
<i>Static Eyes Closed</i>			
f(z) symmetry	46.27	50.62	0.50
f(x) symmetry	49.41	48.02	.56
min com-cop diff symmetry	54.42	48.98	0.77
<i>Static Eyes Open and Arm Abducted</i>			
f(z) symmetry	46.41	50.97	0.88
f(x) symmetry	47.72	48.38	0.99
min com-cop diff symmetry	55.47	51.12	0.50
<i>Static Eyes Closed and Arm Abducted</i>			

f(z) symmetry	45.42	52.58	0.26
f(x) symmetry	50.35	47.29	0.84
min com-cop diff symmetry	55.55	48.45	0.21
<i>Sit-to-stand</i>			
f(z) peak symmetry	42.11	47.98	0.61
f(z) standing symmetry	44.80	50.30	0.19
f(x) peak symmetry	50.67	49.60	0.76
f(x) standing symmetry	53.21	49.90	0.14
min com-cop diff symmetry	52.64	48.71	0.48
<i>Rise-to-walk</i>			
f(x) symmetry	52.00	59.73	0.59
min com-cop diff symmetry	54.30	44.56	0.37
<i>Gait Initiation</i>			
f(z) symmetry	49.12	48.59	0.98
f(x) symmetry	43.38	46.70	0.96
f(y) symmetry	53.60	51.27	0.50
min com-cop diff symmetry	59.21	49.05	0.26

Table 11 – Patients operated on for ankle fractures: Treadmill vs EWB group means and differences in the gait analysis and GRFs results at 3 months evaluation. Significance for U Mann-Whitney test.

ANKLE	Treadmill (mean)	EWB (mean)	Significance
<i>Walk</i>			
Step length	60.00	60.50	0.66

Step speed	0.77	0.88	0.88
Step time symmetry	49.24	49.45	0.92
f(z) symmetry	49.58	49.49	0.61
f(z) variability	43.86	43.17	0.74
min com-cop diff symmetry	53.73	46.49	0.55
f(x) symmetry	52.15	60.52	0.74
f(y) symmetry	46.08	50.86	0.65
<i>Static Eyes Open</i>			
f(z) symmetry	50.18	49.34	0.94
f(x) symmetry	50.13	53.07	0.99
min com-cop diff symmetry	52.32	52.28	0.69
<i>Static Eyes Closed</i>			
f(z) symmetry	49.49	49.73	0.71
f(x) symmetry	48.20	53.40	0.042*
min com-cop diff symmetry	51.17	52.26	0.62
<i>Static Eyes Open and Arm Abducted</i>			
f(z) symmetry	50.92	49.77	0.63
f(x) symmetry	46.83	52.43	0.60
min com-cop diff symmetry	51.48	48.77	0.50
<i>Static Eyes Closed and Arm Abducted</i>			
f(z) symmetry	51.60	50.15	0.54
f(x) symmetry	47.45	52.83	0.78
min com-cop diff symmetry	50.91	51.71	0.10
<i>Sit-to-stand</i>			
f(z) peak symmetry	47.29	49.42	0.85

f(z) standing symmetry	49.73	48.60	0.89
f(x) peak symmetry	50.33	51.32	0.56
f(x) standing symmetry	50.84	51.78	0.81
min com-cop diff symmetry	51.89	52.90	0.64
<i>Rise-to-walk</i>			
f(x) symmetry	54.82	63.70	0.62
min com-cop diff symmetry	52.43	49.27	0.50
<i>Gait Initiation</i>			
f(z) symmetry	47.92	48.87	0.81
f(x) symmetry	42.78	47.86	0.87
f(y) symmetry	52.47	51.51	0.68
min com-cop diff symmetry	53.05	54.85	0.86

3.3.4 Discussion

This study investigated the adjunctive use of an anti-gravity treadmill combined with non-immersive virtual reality (VR) in the rehabilitation of patients recovering from complex lower limb fractures. Early weight-bearing restrictions, often prescribed by surgeons, present a significant challenge for delivering effective rehabilitation during a critical period of recovery. The anti-gravity treadmill addresses this clinical gap by enabling patients to practice walking movements without full weight transfer on the injured limb, thus providing a safe environment for early motor practice. This approach aligns with previous findings by Patil et al. (2013) and Henkelmann et al. (2021), who demonstrated that anti-gravity treadmills reduce joint loading while preserving natural gait mechanics, facilitating early mobilization without jeopardizing tissue healing.

The addition of non-immersive VR further enhances this rehabilitation method by creating an engaging environment that shifts patients' attention away from the conscious control of their injured limbs, common among patients reliant on crutches and focused on safety concerns. This attentional shift likely promotes a return to more automatic and natural gait patterns, closer to pre-injury motor behavior, which is an important rehabilitation goal. Neurocognitive engagement strategies similar to VR have shown benefits in motor learning and functional outcomes in both stroke and orthopedic populations (Krakauer, 2006; Holden, 2005). Therefore, the implicit motor control promoted by VR may underpin the favorable functional outcomes observed in the treadmill group.

Our results suggest that the anti-gravity treadmill intervention supports satisfactory clinical and functional recovery while potentially reducing the duration of conventional physiotherapy, without compromising load management. Specifically, patients recovering from ankle fractures appeared to regain a more accurate perception of limb symmetry, consistent with Jansen et al. (2017), who reported improved proprioceptive accuracy and load distribution in ankle fracture patients undergoing early mobilization protocols.

All participants achieved full independence in activities of daily living (ADLs) by three months post-surgery. Moreover, a higher proportion of patients with tibial plateau fractures treated using the treadmill protocol (Treadmill TIBIA) returned to work compared to those in the early weight-bearing (EWB TIBIA) group. These findings indicate potential benefits of this novel rehabilitation strategy in both functional recovery and socio-economic reintegration, echoing Fawley et al.'s (2024) emphasis on early functional restoration as a key factor for return-to-work outcomes.

Pain scores and joint range of motion (ROM) correlated with improvements in functional scales, with no clinically significant differences detected in WOMAC scores

between early and late follow-up (T1 to T3). The Treadmill TIBIA group started with a significantly lower baseline WOMAC score compared to the EWB TIBIA group, suggesting differences in initial injury severity or patient characteristics that may have influenced recovery trajectories. This baseline imbalance warrants cautious interpretation of comparative outcomes and reflects a common challenge in observational studies, where patient heterogeneity can confound results (van den Ende et al., 2006).

The progression of joint mobility was assessed by examining total ROM, defined as the sum of flexion and extension. In the treadmill group for tibial fractures, ROM showed a consistent improvement over time, with clinically meaningful gains evident by the three-month follow-up. Although six-week assessments revealed limitations due to ongoing orthosis use and weight-bearing restrictions, substantial mobility recovery was observed by the intermediate evaluation. By six months, ROM values approached functional thresholds compatible with independent daily activities and return to work. These trends suggest that the combination of anti-gravity treadmill therapy and VR exercises may positively influence knee joint recovery, providing safe, early joint stimulation without compromising surgical outcomes.

A similar but more gradual pattern was observed in the Treadmill ANKLE group. Mobility remained limited at six weeks, in line with standard immobilization protocols, with a marked increase in ROM occurred between six weeks and three months, coinciding with progression to full weight-bearing. By six months, most patients regained sufficient functional ROM to support independent walking and light recreational activities, although individual variability persisted.

Together, these findings support the hypothesis that combining anti-gravity treadmill therapy with interactive VR environments enhances joint recovery in patients with complex

lower limb fractures. This approach is particularly advantageous when early conventional weight-bearing is contraindicated, as it enables meaningful movement practice within a protected and progressively challenging rehabilitation framework.

Pain reduction, as measured by the Numerical Rating Scale (NRS), showed a steady decline in both groups, confirming effective pain management and the tolerability of the combined treadmill and VR program. The progressive decrease in pain paralleled functional improvements and increased patient-reported independence, suggesting that early mobilization under protected loading does not cause prolonged discomfort or delayed recovery.

Gait analysis conducted at three months postoperatively, when patients generally resume full weight-bearing and daily activities (Santini et al., 2023), provided insight into functional recovery with minimal confounding from early postoperative restrictions. While no statistically significant differences were found between treadmill and EWB groups, biomechanical data suggested trends worth further investigation. Patients in the treadmill tibial fracture group (Treadmill TIBIA) exhibited reduced load perception on the operated limb, although differences were not statistically significant. Reduced step time symmetry and step length in this group may relate to limited knee ROM, contributing to suboptimal gait parameters and highlighting the need for targeted interventions to improve knee mobility. This observation aligns with recent studies which highlighted persistent gait asymmetries in patients with tibial plateau fractures. Fändriks et al. (2024) observed pronounced side differences between injured and non-injured legs two years post-fracture, with impaired knee extension and power generation in the injured leg. Similarly, Fändriks et al. (2021) reported limitations in walking patterns and knee extension three months after injury. Elsåe & Larsen (2017) found significant gait asymmetries in step length, single-support time and swing time one year post-treatment. These asymmetries were associated with reduced health-related quality of life.

Ground reaction force (GRF) data, though lacking statistical significance, indicated subtle differences in neuromuscular strategies or weight-shifting patterns that merit further study. In particular, the Treadmill ANKLE group demonstrated greater medio-lateral GRF symmetry and a smaller minimum distance between the center of pressure (COP) and center of mass (COM). Interestingly, the medial shift of GRF on the operated foot and the tendency to bring the COM closer to the contralateral limb's COP diverge from the lateralized loading patterns typically reported after injury (Mirando et al., 2022).

During dynamic tasks such as rise-to-walk, both treadmill groups exhibited less lateralization of GRF in the medio-lateral direction compared to the EWB groups, despite reduced COP-COM distance toward the contralateral side. These findings suggest that treadmill training may promote more balanced postural control strategies, consistent with a 10-week treadmill walking program by Pereira et al., (2020) where postural balance significantly improved.

Functional tasks including sit-to-stand, rise-to-walk and gait initiation showed similar performance and GRF symmetry across groups, indicating both rehabilitation approaches effectively facilitate coordinated whole-body movements and dynamic postural control.

During walking, all treadmill patients showed reduced GRF symmetry along the antero-posterior axis, with lower loading on the operated limb, as protective strategy after lower limb fractures described in prior biomechanical studies (Mirando et al., 2022; Warmerdam et al., 2023). Despite this, vertical GRF peak-to-peak distances were similar across groups, reflecting adequate load management during stance. These findings suggest that although subtle asymmetries persist, patients maintain sufficient functional control to support recovery and daily activities, consistent with previous research emphasizing progressive motor control improvements during early rehabilitation (Elbaz et al., 2016; van Hove et al., 2019).

This study's non-randomized, single-center design limits causal inference and introduces potential confounding, including selection bias and lack of blinding. This study has several limitations that should be considered when interpreting the results. The non-randomized design may have introduced selection bias, as patients were assigned to groups based on clinical criteria rather than randomly, potentially leading to differences in baseline characteristics that influenced recovery outcomes. For instance, the Treadmill TIBIA group presented with lower baseline disability scores (WOMAC), which may have influenced the comparative analysis with the early weight-bearing group. Additionally, as WOMAC is a self-administered questionnaire, there is a potential for reporting bias, where patients might underestimate or overestimate their symptoms due to subjective perception or social desirability. This response bias could have led to an underestimation of disability severity in the Treadmill group, thus affecting the accuracy of baseline comparisons and subsequent outcome interpretations.

Being a single-center study, the findings may not be fully generalizable to other clinical settings with different protocols and expertise. Moreover, the lack of blinding could have influenced patient behavior, therapist interaction and outcome assessments, introducing performance and detection biases.

There is also the possibility of attrition bias due to incomplete follow-up data, which might have affected the results if dropout rates differed between groups. Additionally, uncontrolled factors such as rehabilitation intensity, patient adherence and psychosocial influences were not fully accounted for and may have impacted recovery.

The relatively small and heterogeneous sample size limits statistical power, increasing the chance of missing significant effects and reducing the precision of subgroup analyses. Lastly, the follow-up period focused on short to medium-term outcomes, so the long-term sustainability of improvements remains uncertain.

Future research should confirm these findings through randomized controlled trials with larger samples and standardized protocols. Investigating optimal duration, intensity and integration of VR in anti-gravity treadmill rehabilitation could refine treatment. Additionally, incorporating electromyography (EMG) may objectively verify the intervention's benefits in mitigating muscle mass loss after surgical fixation, providing insight into neuromuscular activation patterns critical for preserving muscle integrity and promoting recovery. Finally, exploring long-term outcomes and cost-effectiveness will be essential for informing clinical decision-making and resource allocation.

In summary, the present gait analysis suggests that treadmill training combined with non-immersive VR achieves functional gait outcomes comparable to early full weight-bearing protocols, despite more restrictive initial loading and greater fracture severity. Trends toward improved step symmetry and vertical loading in the Treadmill groups highlight its potential advantage in promoting balanced gait restoration. Although most differences did not reach statistical significance, consistent functional recovery and the absence of adverse effects support the clinical feasibility and safety of this combined rehabilitative approach.

3.4 Study 3: Early rehabilitation with Motor Imagery in patients with lower limb fractures undergoing conservative treatment: a pilot study

Abstract

This study explores the effectiveness of Motor Imagery (MI) in early rehabilitation for patients with lower limb fractures during the immobilization phase. The rationale stems from the known negative effects of prolonged immobilization, such as muscle atrophy, cortical changes and delayed return to function and the need for early, accessible interventions.

Participants with conservatively treated fractures were divided into two groups: one performed guided MI exercises during immobilization in addition to standard care, while the control group followed usual rehabilitation after cast removal. The findings showed that those in the MI group required significantly fewer supervised physiotherapy sessions to regain function, without compromising outcomes. They also experienced reduced pain and lower levels of movement-related fear (kinesiophobia).

Kinetic gait analysis revealed more symmetrical loading in the MI group, suggesting that motor patterns were better preserved despite immobilization. Importantly, this approach does not rely on surgical intervention or specialized equipment, making it accessible to any physiotherapist trained in MI techniques.

These results highlight the potential of MI as a simple, cost-effective strategy to support motor recovery in fracture rehabilitation. Future research, particularly randomized controlled trials, is needed to confirm these promising outcomes and define the best protocols for clinical practice.

3.4.1 Introduction

Conservative treatment of ankle and metatarsal fractures requires a period of immobilization of 4-6 weeks to allow to ensure adequate fracture healing (Grosset et al., 2008; Bica et al., 2016). Immobilization, commonly achieved through casts or splints, significantly restricts the lower limb's ability to contribute to postural control and balance (Ikeda et al., 2023; Elam et al., 2022).

While the literature have demonstrated the benefits of prescribing minimal weight-bearing such as toe-touch loading to preserve lower limb movement patterns (Westerman et al., 2008), patient adherence to these protocols remains suboptimal, with non-compliance rates reported as high as 40% (Ruiz et al., 2014; Lajevardi-Khosh et al., 2019).

Experimental models of temporary immobilization and sensorimotor deprivation (Avanzino et al., 2011; Karita et al., 2017; Huber et al., 2006; Moisello et al., 2008) have demonstrated that even brief periods of disuse can rapidly induce functional and structural changes within the nervous system.

Temporary limb immobilization induces significant changes in both the musculoskeletal and nervous systems, as highlighted by neurophysiological studies. Muscular effects include atrophy, decreased protein synthesis and reduced electromyographic (EMG) activity (Booth, 1982). In the nervous system, immobilization leads to a decrease in cortical thickness in contralateral sensorimotor areas of the brain and decreased the fractional anisotropy of the corticospinal tract (Langer et al., 2012).

Such neural changes are associated with deficits in inter-joint coordination and postural control with potential long-term implications for movement quality (Maidan et al., 2021).

To mitigate these effects, several neurocognitive rehabilitation strategies have been proposed. Action Observation Therapy (AOT) (Buccino, 2014; Bellelli et al., 2010; Ertelt et al., 2007) and Motor Imagery (MI) (Dilek et al., 2018; McGee et al., 2018; Dickstein et al.,

2007; Malouin et al., 2003) are increasingly utilized to maintain motor representations in both central and peripheral conditions. MI represents a sophisticated cognitive process characterized by the internal rehearsal of motor actions without any visible movement (Decety, 1996; Abbas et al., 2011) that activates sensory-motor brain regions also involved in actual movement (Munzert et al., 2009), including the premotor cortex, supplementary motor area, parietal cortex, basal ganglia and cerebellum (Jeannerod, 2001; Hardwick et al., 2017; Lotze and Halsband, 2006). MI shares overlapping neural pathways with motor control processes, suggesting that it may serve as an unconscious preparatory mechanism for motor actions (Abbas et al., 2011).

Its efficacy in promoting motor learning, enhancing neuroplasticity and improving performance is well documented in both healthy individuals and those within clinical populations (Moran & O'Shea, 2020; Mulder, 2007), with a critical role played by prefrontal and basal ganglia circuits in sustaining dynamic motor representations during MI, facilitating the process of internal rehearsal (Decety, 1996; O'Shea, 2022).

MI encompasses various modalities, including visual, auditory and kinesthetic imagery, each of which can be effectively integrated and utilized within the contexts of motor learning and rehabilitation (Guillot et al., 2014).

Motor imagery can be subdivided into kinesthetic (KMI) and visual (VMI) forms. KMI involves mentally simulating a movement while experiencing the sensation of muscle contractions and physical feedback, as though the movement were actually being performed, from a first-person perspective (Stinear et al., 2006). VMI is the process of visualizing oneself performing the movement from an external perspective, as if observing it from an external viewpoint. VMI predominantly engages the posterior cingulate and frontopolar cortex, supporting the conceptual distinction between internal and external modes of imagery (Yang et al., 2021).

KMI may be more effective than VMI for improving performance, as seen with the use of brain-machine interface decoders. However, without clear instructions, individuals may struggle to effectively apply the appropriate imagery strategy, leading to confusion (Yang et al., 2021).

Stinear et al. (Stinear et al., 2006) demonstrated that kinesthetic motor imagery (KMI), but not visual motor imagery (VMI), modulates corticomotor excitability, particularly at the supraspinal level. This suggests that the type of motor imagery significantly impacts the extent of neural activation, with KMI potentially offering greater benefits for motor learning. KMI involves imagining the sensation of performing a movement with all its sensory feedback from a first-person perspective, while VMI involves visualizing oneself performing the action from a third-person perspective, as if watching from a distance.

Other studies (Ruby and Decety, 2003; Guillot et al., 2009) also explored these two forms of imagery, finding that both activated common brain areas, including the supplementary motor area (SMA), precentral gyrus and precuneus. However, KMI led to increased activation in regions such as the left inferior parietal lobule and the left somatosensory cortex, while VMI activated the right inferior parietal lobule, posterior cingulate and frontopolar cortex.

These findings underscore the distinction between internal (first-person, kinesthetic) and external (third-person, visual) imagery. Internal imagery replicates the sensory experience of movement, making it more effective for motor learning, whereas external imagery involves observing oneself performing the movement, comparable to watching another person.

Motor imagery (MI) is frequently employed in rehabilitation following central nervous system injury: for example, when combined with conventional therapy, motor imagery shows considerable promise in addressing upper limb motor deficits after stroke (Fernandez-Gomez & Sánchez-Cabeza, 2018).

However, international literature also includes studies showing that motor imagery can be influenced by even short periods of immobilization (Burianova et al., 2016) and how it can be effectively utilized in cases of musculoskeletal system pathology. Research indicates that temporary limb immobilization can alter neural representations of movement, potentially diminishing the accuracy and vividness of MI (Burianova et al., 2016). Burianova et al.'s study (Burianova et al., 2016) examined human brain neuroplasticity, specifically focusing on the effects of motor imagery (MI) after a short period of hand immobilization. Using advanced neuroimaging techniques such as functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG) to assess changes in neural oscillations and transcranial magnetic stimulation (TMS) to measure corticospinal excitability, the researchers found that even 24 hours of immobilization led to significant changes in sensorimotor region excitability and motor processing. The study revealed that immobilization not only impacts actual motor execution but also alters the neural networks involved in motor imagery. This suggests that immobilization disrupts both physical motor functions and the cognitive processes underlying motor imagery formation.

Despite this, MI can attenuate disuse-related deficits and has been successfully applied in rehabilitation protocols for musculoskeletal injuries, helping patients maintain motor representations and prevent the adverse effects of disuse, such as muscle atrophy and decreased coordination. A study by Lebon (Lebon et al., 2010) investigated whether motor imagery (MI) could enhance strength in both the upper and lower limbs. The findings indicated that combining MI with physical training significantly increased lower limb strength without causing structural changes in the muscle. Moreover, the study hypothesized that MI might boost motivation and confidence in performing motor tasks, which could positively influence the technical aspects of actual movement execution.

A randomized controlled trial conducted by Birinci et al. in 2022 (Birinci et al., 2022) investigated the efficacy of Graded Motor Imagery (GMI), which comprises a combination of left-right discrimination, motor imagery and mirror therapy, in patients with post-traumatic elbow fractures. The findings indicated that the GMI approach resulted in significantly greater improvements in joint range of motion, strength and a reduction in pain and fear of re-injury (measured using the *Tampa Scale of Kinesiophobia*) compared to a group receiving structured exercise alone.

A previous study by Dilek (Dilek et al., 2018) explored the impact of combining GMI with physiotherapy on hand function recovery in patients with distal radius fractures. The results showed that the inclusion of MI in the treatment regimen led to notable benefits, including improved pain and edema management, as well as increased grip strength by the end of the therapy sessions.

A German study by Mayer et al. (2005) examined the effects of *mental gait training* in patients who underwent hip arthroplasty. The findings indicated that the use of motor imagery, based on personalized kinesthetic motor imagery, significantly improved parameters such as stride length and kinematic variables in the intervention group compared to the control group.

Despite promising evidence, the clinical application of MI remains inconsistent, often limited by the lack of operational guidelines (Bovend'Eerd et al., 2012).

A complementary approach, AOT, has demonstrated efficacy in both neurological and orthopedic populations by evoking internal representations through video-based observation (Pelosin et al., 2010; Franceschini et al., 2012). AOT progressively introduces increasingly complex movement sequences, reinforcing real-world motor patterns through perceptual priming.

AOT has been shown to be a useful tool in post-stroke rehabilitation and in managing freezing of gait symptoms in patients with Parkinson's disease (Pelosin et al., 2010), by

implicitly evoking the internal representation of movement. In Pelosin et al.'s study, patients were presented video clips showing strategies to overcome freezing of gait, progressively increasing the complexity of the observed actions, from simpler actions to more complex movements. Similarly, in a study involving patients after orthopedic surgery (Bellelli et al., 2010), AOT was used by presenting a range of actions, from simple lower limb movements on a bed to more complex tasks such as climbing stairs or cycling. These examples highlight the importance of rehabilitation strategies that facilitate the activation of cortical representations, bringing them closer to real actions in ecological settings.

This study proposes the integration of Motor Imagery within the rehabilitation framework based on Cognitive Multisensory Rehabilitation (Van de Winckel et al., 2020), aiming to offer patients a personalized, imagery-based training approach rooted in their pre-injury motor experiences. This integration seeks to maintain cortical motor representations during immobilization, thereby reducing the functional impact of disuse and optimizing recovery outcomes.

To evaluate the effectiveness of this approach, patients will be assessed following cast removal, at the time of early mobilization, through gait analysis and other standardized motor tasks. These assessments will be compared to those of a control group who did not perform motor imagery during immobilization. The comparison aims to determine whether movement alterations can already emerge after just one month of immobilization and whether early engagement in motor imagery can mitigate or prevent such deficits. By analyzing biomechanical and functional performance indicators, the study will explore the potential of motor imagery to preserve motor control and reduce maladaptive compensatory patterns often observed after prolonged joint disuse.

3.4.2 Materials and Methods

This pilot study is conducted in collaboration with the Department of Orthopaedics and Traumatology at Cattinara Hospital (ASUGI) in Trieste, Italy. All clinical and biomechanical evaluations take place at the Motion Analysis Laboratory of the Physiotherapy Degree Program at the University of Trieste. The laboratory is equipped with eight high-speed infrared cameras and four centrally embedded force platforms, which are calibrated prior to each acquisition session. These devices allow for the synchronized collection of kinematic and kinetic data during barefoot walking and functional tasks performed along a 10-meter walkway, simulating daily life activities such as standing, transitioning from sitting to standing, rise-to-walk, gait initiation and steady-state walking.

Participants are recruited among adult patients (aged 18 to 65) who have sustained simple fractures of the lower limb, such as ankle or metatarsal fractures and are undergoing conservative treatment involving absolute immobilization with a cast or brace for at least three weeks. Patients are excluded if they have a history of neurological or psychiatric disorders, substance abuse, or alcohol dependency.

Before enrollment, all eligible individuals receive detailed information regarding the study's purpose, treatment modalities and rehabilitation protocols and provide written informed consent in accordance with the EU General Data Protection Regulation (GDPR 2016/679).

Patients are randomly assigned in a 1:1 ratio to either an experimental group (Motor Imagery) receiving early motor imagery-based rehabilitation or a control group (Controls) following the standard regional clinical care pathway. Those in the control group begin physiotherapy only after cast removal, whereas participants in the motor imagery group initiate their intervention within the first week of immobilization.

Patients in the intervention group first complete the Kinesthetic and Visual Imagery Questionnaire-10 (KVIQ-10) (Malouin et al., 2017), which assesses their ability to generate visual and kinesthetic motor imagery across in response to proposed movements for various body regions (shoulder, hand, trunk, hip, foot) on both the dominant and non-dominant sides. Based on their individual imagery profiles, they begin a structured program grounded in the principles of Cognitive Multisensory Rehabilitation (CMR) (Van de Winckel et al., 2020). Initially, the program emphasizes the generation of visual and kinesthetic motor imagery for the immobilized limb in the absence of physical movement. These early sessions are performed in supine, sitting and standing positions.

The proposed exercises are based on Cognitive Multisensory Rehabilitation (Van de Winckel et al., 2020) and involve problem-solving techniques to prompt the patient to identify the correct movement to complete the given perceptual tasks. Given the immobilization device, exercises primarily focus on perceptual tasks involving the hip and knee, with an emphasis on maintaining patients' awareness of how these segments interact with the foot during typical activities. For instance, a knee flexion-extension position recognition exercise requires continuous integration of knee position information with the sense of the foot's position in relation to the body (e.g., closer or farther).

As the sessions progress, patients engage in increasingly complex exercises designed to maintain and refine the mental representation of limb function. For example, they are asked to recognize and imagine knee flexion or extension while mentally integrating the perceived position of the foot relative to the trunk. Imagery is first practiced using the contralateral limb and then transferred to the immobilized limb, always encouraging the patient to experience the movement "as if" the injured side were free to move naturally. Therapists monitored whether patients predominantly evoke visual or kinesthetic imagery and provided guidance to reinforce the kinesthetic component by drawing on sensory experiences from the unaffected side. Each

session concludes with a reflective task in which the patient identifies everyday activities that might involve movements similar to those just practiced, promoting contextual and multisensorial integration of the imagined motor sequences and further strengthening the internal representation of pre-injury movement patterns.

Box 1 provides a brief description of the progression of exercises using motor imagery.

Box 1 - Progression of treatment with Motor Imagery during rehabilitation.

1	Evocation of visual motor imagery: visualization of the immobilized limb by transferring the visual image of the contralateral limb.
2	Kinesthetic imagery: the image of single-joint movements or the sensations of touch and kinesthesia derived from comparison with the contralateral limb.
3	Proposal for CMR exercises, both with the immobilized limb and with the contralateral limb, to enhance kinesthetic motor imagery.
4	Comparison between exercises and the actual functions of the lower limb and walking.
5	Enrichment of kinesthetic imagery through the representation of pre-injury actions, not related to the rehabilitation context.

Patients in the control group receive no intervention during the immobilization period and started physical therapy after cast removal, according to standard clinical timelines. No motor imagery strategies are introduced to this group.

All participants are assessed at two follow-up intervals (six weeks and three months post-injury) using a combination of biomechanical, clinical and patient-reported outcome measures. Biomechanical assessments are conducted at the Motion Analysis Laboratory and include both static and dynamic tasks designed to study balance and gait. These tasks are performed barefoot and include quiet standing with eyes open and closed, sit-to-stand transitions, rise-to-walk, gait initiation and continuous walking. Data on ground reaction forces (GRFs) are collected and normalized to each participant's body mass and limb length. Symmetry indices are calculated to quantify interlimb differences in load distribution, while spatiotemporal parameters such as step length and walking velocity are derived. The trajectory of the center of mass relative to the center of pressure (COM–COP) is analyzed to assess postural control and dynamic stability (*see 3.1 General Methods for details*).

Clinical and patient-reported outcome measures are used to assess functional recovery in patients with foot and midfoot fractures. Specifically, the American Orthopaedic Foot and Ankle Society (AOFAS) score (Kitaoka et al., 1994) and the Olerud-Molander Ankle Score (OMAS) (Olerud & Molander, 1984) are administered. Pain intensity is measured with the Numeric Rating Scale (NRS) (Jensen et al., 1986; Hjerstad et al., 2011) and self-perceived functional independence in activities of daily living (ADLs), return to work and return to sport are investigated.

Additionally, patients are evaluated for kinesiophobia, defined as the fear of sustaining new injuries post-fracture or the fear of movement/reinjury. This is assessed using the Tampa Scale for Kinesiophobia (TSK) (Vlaeyen et al., 1995), a tool previously applied in the literature for similar patient groups (Bello et al., 2020). The TSK has also been translated, culturally adapted and validated for use in Italian populations (Monticone et al., 2016). Previous research has explored the potential of motor imagery treatment to reduce fear of movement (Candiri et al., 2023; Salik Sengul et al., 2021). However, it's important to note that these studies primarily

involved patients undergoing interventions such as knee arthroplasty and lumbar spinal surgery, thus often having a history of chronic illness prior to the procedure.

All patients are evaluated at 6 weeks and 3 months post-fracture with motion analysis conducted at the motion analysis laboratory of the Physiotherapy Bachelor's Degree Program at the University of Trieste, during the execution of six tasks: static balance with eyes open and eyes closed, static balance with abduction of the limb ipsilateral to the fracture site with eyes open and eyes closed, sit to stand, rise to walk, gait initiation and gait (*see 3.1 General Methods for details*).

All collected data are anonymized and securely stored on offline, password-protected systems accessible only to authorized research personnel. Statistical analyses are performed using Jamovi software, version 2.3.18.0. Between-group differences are analyzed using the Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables, with statistical significance defined as $p < 0.05$. Only complete-case data are included in the analyses and no imputation is performed for missing data. This methodological decision preserves the internal validity of the findings but may limit external generalizability if data were not missing completely at random.

The design of this study incorporates the potential for performance bias, primarily stemming from the unblinded nature of the intervention. Both the individuals participating and the therapists providing the motor imagery intervention are aware of group assignments. This absence of blinding implies that participants' expectations, levels of effort, or even subtle psychological reactions might have influenced their engagement and the outcomes they reported. Likewise, the therapists' awareness of group allocations could have subtly and unconsciously, affected their interaction style, encouragement, or specific aspects of treatment delivery, potentially leading to variations in care beyond the intended intervention.

A moderate risk of detection bias exists concerning the outcome assessments: the collection and interpretation of clinical and patient-reported outcome measures (including AOFAS, OMAS, NRS and TSK scores, along with self-reported activities of daily living, return to work and sport) could be affected if the individuals conducting the assessments were not blinded to the participants' group assignments. Unconscious biases in how data are assessed or interpreted might subtly incline results toward anticipated outcomes.

Finally, the deliberate choice to include only complete-case data in the statistical analyses, without employing imputation for missing values, is made to protect the internal validity of the study's conclusions. This approach ensures that findings are derived directly from observed measurements, thereby reducing the potential for bias often associated with imputation methods. This methodological stance could introduce attrition bias if there are systematic differences between patients with complete data and those with missing data, particularly if the data are not missing entirely at random. Consequently, this selective inclusion might restrict the external generalizability of the findings to the wider population of individuals with lower limb fractures.

3.4.3 Results

A total of 20 patients with simple lower limb fractures treated conservatively with casting or bracing were enrolled in this feasibility study. Participants were randomly assigned to either the Motor Imagery (MI) group or the Control group in a 1:1 ratio. The mean age of participants in the MI group was 45.4 years (SD = 11.9), while the mean age in the Control group was 52.11 years (SD = 11.9). No statistically significant differences were observed between the two groups in terms of age, type of fracture, or other baseline demographic characteristics, confirming adequate comparability at baseline.

A significant difference was observed in the average number of physical therapy sessions completed by each group during the study period. Patients in the Motor Imagery group attended an average of 6.2 sessions (min=2, max=10), markedly fewer than the Control group, which averaged 14.44 sessions (min=10, max=30) ($p=0.0007$).

Results reported at six weeks post-fracture correspond to a time point when all participants had transitioned out of their cast or brace and had initiated rehabilitation for the functionality of the affected lower limb. No patient experienced any clinical complications related to the study's proposed treatments. Furthermore, all patients across both study groups were able to bear full weight on their fractured limb by this 6-week assessment.

Self-perceived functional independence in daily activities showed a trend, with one patient (10%) in the Motor Imagery group reporting not feeling autonomous, compared to two patients (20%) in the Controls group.

Regarding return to work, six patients in the MI group had resumed employment, whereas three patients in the control group had returned to their jobs, a difference that was not statistically significant ($p=0.36$ for Fisher's exact test). Similarly, concerning participation in pre-fracture sports and recreational activities, three patients in the MI group had resumed such activities, while only one patient in the control group reported engaging in sports ($p=0.58$ for Fisher's exact test).

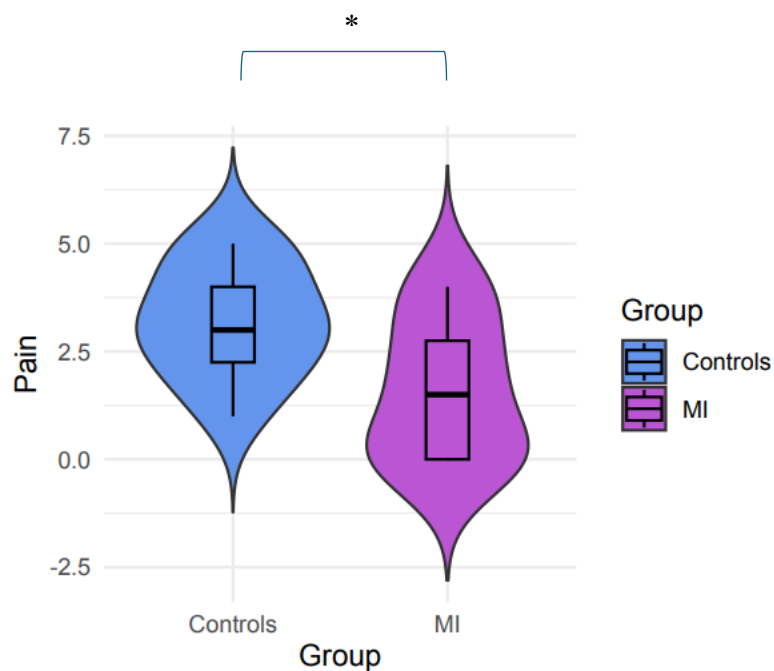
The average scores from self-administered clinical questionnaires at the six-week evaluation are presented in *Table 12*. No statistically significant differences were found between groups for the Olerud-Molander Ankle Score (OMAS) or the American Orthopaedic Foot and Ankle Society (AOFAS) score. The mean OMAS score was 70 for the Motor Imagery group and 57.22 for Controls ($p=0.22$), while mean AOFAS scores were 83 for the MI group and 74.22 for controls ($p=0.36$).

Table 12 - Average scores of responses to the OMAS and AOFAS questionnaires for the Motor Imagery (MI) and Controls groups at six weeks post-fracture. Significance was assessed using the Mann-Whitney test.

	Motor Imagery	Controls	Significance
OMAS	70	57.22	0.22
AOFAS	83	74.22	0.36

Pain intensity, assessed using the Numeric Rating Scale (NRS), showed a marginal statistical difference between the two groups at six weeks, as illustrated in *Figure 16*, with $p=0.05$.

Figure 16 - Violin plot illustrating the values reported by patients in the two groups regarding the average pain item (NRS 0-10) at six weeks post-fracture. Significance assessed using the Mann-Whitney test: $p = 0.05$.



Evaluation of kinesiophobia, using the Tampa Scale for Kinesiophobia (TSK), revealed a statistically significant difference between the groups at six weeks. As depicted in *Figure 17*, the analysis yielded a $p=0.01778$, indicating that the Motor Imagery group reported significantly lower levels of kinesiophobia compared to the Control group.

Figure 17 - Violin plot illustrating the values reported by patients in the two groups regarding the Tampa Scale for Kinesiophobia at six weeks post-fracture. Significance assessed using the Mann-Whitney test: $p = 0.01778$, indicating statistical significance.

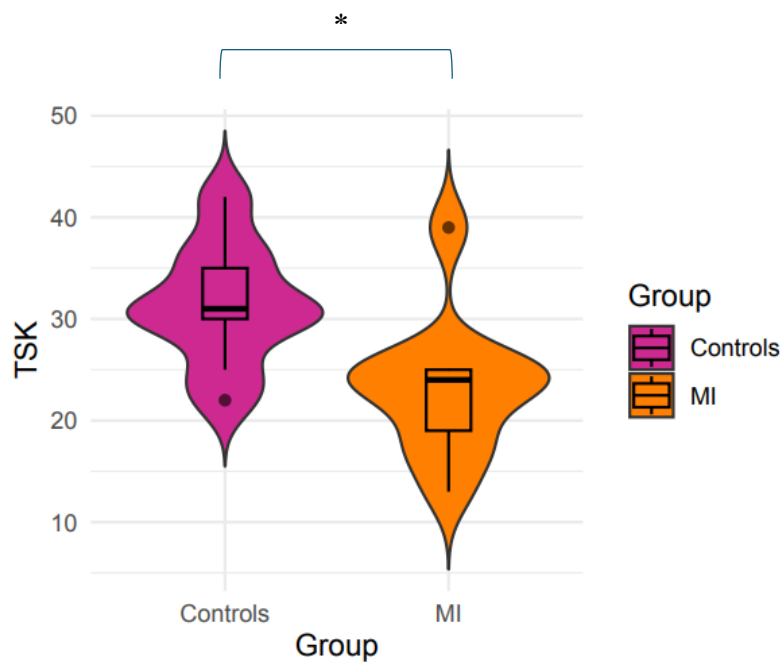


Table 13 summarizes the results from the gait analysis and ground reaction force (GRF) assessments across the different tasks examined. No significant biomechanical differences were observed between the two groups. The only exception was found in the minimum distance between the center of mass (COM) and the center of pressure (COP) during the static test with upper limb abduction while eyes open. In this specific task, the Control group demonstrated a greater proximity of the COM to the COP of the fractured limb compared to

the Motor Imagery group ($p=0.03$). No other tasks, including sit-to-stand, rise-to-walk, gait initiation, or level walking, revealed significant differences between groups in terms of GRF symmetry, variability, or COM-COP dynamics.

All gait and postural data were normalized for body mass and limb length and symmetry indices were computed between the fractured and contralateral limbs.

Table 13 - MI vs Controls group means and differences in the gait analysis and GRFs results at 6-week evaluation. Significance for U Mann Whitney test.

	MI (mean)	Controls (mean)	Significance
<i>Walk</i>			
Step length	0.60	0.55	0.55
Step speed	1.10	0.87	0.92
Step time symmetry	47.76	54.63	0.35
f(z) symmetry	50.02	48.36	0.59
f(z) variability	48.77	34.32	0.52
min com-cop diff symmetry	57.62	57.06	0.77
f(x) symmetry	56.59	49.82	0.46
f(y) symmetry	51.23	45.67	0.34
<i>Static Eyes Open</i>			
f(z) symmetry	48.09	46.25	0.80
f(x) symmetry	52.06	50.75	0.92
min com-cop diff symmetry	49.31	56.20	0.06
<i>Static Eyes Closed</i>			
f(z) symmetry	48.59	46.53	0.95

f(x) symmetry	52.87	48.85	0.75
min com-cop diff symmetry	50.72	56.88	0.18
<i>Static Eyes Open and Arm Abducted</i>			
f(z) symmetry	50.35	46.23	0.24
f(x) symmetry	53.10	49.89	0.97
min com-cop diff symmetry	50.31	57.58	0.03*
<i>Static Eyes Closed and Arm Abducted</i>			
f(z) symmetry	50.27	46.09	0.35
f(x) symmetry	54.95	47.74	0.92
min com-cop diff symmetry	51.73	55.93	0.35
<i>Sit-to-stand</i>			
f(z) peak symmetry	48.01	44.36	0.63
f(z) standing symmetry	49.70	44.16	0.14
f(x) peak symmetry	51.52	54.83	0.90
f(x) standing symmetry	51.59	51.72	0.68
min com-cop diff symmetry	49.53	54.75	0.88
<i>Rise-to-walk</i>			
f(x) symmetry	55.19	61.42	0.31
min com-cop diff symmetry	50.21	52.34	0.76
<i>Gait Initiation</i>			
f(z) symmetry	48.72	48.48	0.92
f(x) symmetry	46.52	43.65	0.88
f(y) symmetry	51.79	52.51	0.88
min com-cop diff symmetry	47.80	58.07	0.29

3.4.4 Discussion

This pilot study aimed to investigate the effects of an early rehabilitation program, initiated while the fractured limb remained immobilized in a cast or brace, on functional recovery following lower limb fractures. The preliminary results offer valuable insights into the practical application and early impacts of integrating Motor Imagery (MI) into acute fracture management.

Although the total number of rehabilitative sessions was not pre-defined as a primary outcome, a significant difference was observed between the MI and control groups ($p=0.0007$). Patients in the MI group frequently requested to perform motor imagery exercises independently at home, which directly led to a reduction in supervised physiotherapy sessions. This aligns with previous research suggesting that MI can enhance patient self-efficacy (Cuenca-Martínez et al., 2022), potentially empowering individuals to engage more autonomously in their rehabilitation without compromising safety or adherence. This contrasts with a previous rehabilitation protocol with intensive therapist supervision to maintain patient adherence (Bovend'Eerd et al., 2012).

The MI group's inclination towards home-based practice mirrors trends observed in stroke rehabilitation, where MI has been shown to reduce reliance on clinical resources without compromising patient outcomes (Donati et al., 2024). The absence of dropouts within our MI cohort further underscores its acceptability, which aligns with reports suggesting that MI fosters patient empowerment and adherence (Hu et al., 2025; Tedeschi, 2024). During their physical therapy sessions, MI group patients actively discussed obstacles encountered during home exercises and with physiotherapist support, refined their imagery quality or developed alternative exercises.

While no statistically significant differences were found in functional outcomes measured by the Olerud-Molander Ankle Score (OMAS) and the American Orthopaedic Foot

and Ankle Society (AOFAS) scores at six weeks, the MI group consistently showed higher mean scores on these functional questionnaires. This consistent trend, although not statistically significant in this small pilot study, may suggest a clinically relevant benefit of targeted early therapy for functional recovery, even when patients are unable to perform their usual activities. This observation is consistent with the systematic review by Guerra et al. (2017), where are reported improved motor outcomes and reduced perceived disability in stroke populations practicing MI.

A significant reduction in pain intensity was observed in the MI group ($p=0.05$), a finding potentially attributable to MI's capacity to modulate central pain processing. This aligns with Strauss et al. (2021), who demonstrated that MI reduces activation in cortical regions associated with pain perception, such as the anterior cingulate cortex. The early initiation of rehabilitation treatment and continuous monitoring by a physical therapist during the acute phase following a fracture might also influence psychological factors related to pain perception (Steven et al., 2010), contributing to this observed reduction.

MI appeared to mitigate kinesiophobia, as reflected in significantly lower Tampa Scale for Kinesiophobia (TSK) scores for the MI group ($p=0.0178$). This effect supports the theoretical framework of the fear-avoidance model (Vlaeyen & Linton, 2000), which posits that early cognitive interventions can interrupt maladaptive cycles of fear and disuse. The reduced perception of pain observed in the MI group in this study is also associated with these lower TSK scores, indicating a reciprocal influence between kinesiophobia and pain intensity (Kortlever et al., 2021). Unlike other cohorts in the literature where elevated kinesiophobia scores persist after fracture (Bello et al., 2020), none of the participants in the current study, from either group, exceeded the clinical cutoff for kinesiophobia (TSK score ≥ 37). This

discrepancy may stem from our study's specific focus on acute-phase interventions, which could preempt the consolidation of fear.

Kinematic and kinetic analyses performed using motion analysis did not reveal statistically significant differences between the two groups at the six-week follow-up. This was somewhat unexpected, as a greater difference was anticipated, given that patients typically tend to avoid using the immobilized lower limb during the initial recovery period by relying on crutches and keeping the limb elevated.

Subtle trends emerged: patients in the MI group tended to utilize the fractured lower limb more effectively than those in the control group when managing their support base in both static and dynamic tasks. Their values approached symmetry with the contralateral limb, evident in both the vertical ($f(z)$) and horizontal ($f(x)$ and $f(y)$) ground reaction force components. While many symmetry data points between the two limbs were close to 50% in the MI group, there was a general tendency for the control group to underestimate the ground reaction force management capabilities of the fractured limb, maintaining values below 50% symmetry. This extends Grangeon et al.'s (2012) work on spinal cord injury, where MI preserved interlimb coordination despite immobilization.

The same trend was observed in the difference between the peaks of the vertical ground reaction force ($f(z)$), where the control group demonstrated less (albeit not significant) variability compared to the contralateral limb and the MI group. Additionally, data regarding the minimum COM-COP distance showed a greater tendency for the control group to keep the center of mass (COM) shifted towards the center of pressure (COP) of the contralateral limb, potentially in an effort to achieve greater stability. In contrast, patients in the MI group displayed greater ease in maintaining a nearly symmetrical COM-COP distance relative to the contralateral limb, suggesting enhanced load acceptance, similar to patterns seen in athletes

using MI to maintain sport-specific motor engrams (Gippert et al., 2025). The compensatory COM shifts observed in controls are consistent with strategies associated with prolonged gait asymmetry in metatarsal fracture cohorts (Bauer et al., 1993).

This pilot study has several limitations that warrant consideration. The non-randomized design and small sample size inherently limit the generalizability of these findings. However, it is acknowledged that pragmatic trials in rehabilitation often face similar constraints (Ford et al., 2020). The lack of blinding for participants and therapists may have introduced performance bias, as the cognitive engagement inherent in MI could enhance placebo effects produced by the healthcare context (Rossetini et al., 2020).

Future research should prioritize conducting randomized controlled trials (RCTs) with larger sample sizes to confirm these preliminary findings. It is also crucial to standardize MI protocols using validated tools like the Movement Imagery Questionnaire (MIQ-RS) to objectively quantify imagery vividness. Incorporating advanced neuroimaging techniques such as functional magnetic resonance imaging (fMRI) or magnetoencephalography (MEG) could provide deeper insights into MI's impact on sensorimotor cortex reorganization during periods of immobilization, building on findings from limb disuse.

Despite the limitations, these preliminary results support integrating MI into fracture rehabilitation to potentially bridge the gap between immobilization and functional recovery. The reduced need for supervised sessions aligns with cost-effectiveness priorities in value-based care. Moreover, the observed early mitigation of pain and kinesiophobia may accelerate return to work, a critical socioeconomic outcome for patients. While the motor imagery intervention did not lead to statistically significant improvements in biomechanical markers at this early time point, the improvements in clinical and patient-reported outcomes indicate promising early benefits in terms of pain perception and psychological readiness for recovery.

Chapter 4: General Conclusions

This doctoral thesis has rigorously explored innovative and early rehabilitation approaches for patients recovering from lower limb fractures, aiming to integrate these strategies into a redefined medical framework for functional recovery. Recognizing the limitations associated with prolonged immobilization, such as muscle atrophy and cortical alterations, this work sought to optimize patient outcomes by preserving and enhancing functional capacity, pain management and the prevention of neuromuscular complications, thereby influencing the overall duration of rehabilitation compared to conventional protocols. The underlying philosophy is predicated on the understanding that fracture recovery involves a complex interplay of biomechanical, neurological and psychological factors, all requiring a comprehensive rehabilitation plan. This research was guided by the hypothesis that integrating rehabilitation techniques based on principles of neuroplasticity and sensorimotor control could preserve or even enhance motor function, accelerate return to daily activities and reduce both pain and kinesiophobia.

The strength of this research lies in its unified methodological approach, characterized by consistent inclusion and exclusion criteria and the use of standardized outcome measures across all three observational studies. This framework was intentionally designed to allow for meaningful comparisons across interventions and to identify common threads for clinical practice. Moreover, this work is deeply rooted in contemporary principles of neuroplasticity, sensorimotor control and patient-centered care, which are essential for promoting effective and lasting recovery.

Main Results Obtained

The studies collectively demonstrated clinical and functional improvements associated with early and innovative rehabilitation interventions in patients with lower limb fractures. Although the research was exploratory and feasibility-oriented, several key outcomes emerged.

Functional Recovery and Autonomy

Patients who underwent early weight-bearing protocols (Study 1) exhibited accelerated recovery of autonomy in activities of daily living (ADLs) compared to those following traditional restricted weight-bearing regimens. This was evidenced by improvements reaching clinically meaningful thresholds within the first three months post-surgery on validated functional scales such as the AOFAS and WOMAC. These findings corroborate prior randomized controlled trials and meta-analyses indicating that early mobilization promotes faster restoration of gait and balance without increasing complication rates (Canton et al., 2022). Radiographic follow-up consistently confirmed that early weight-bearing did not compromise bone healing or hardware stability. These findings not only support the adoption of earlier mobilization but also align with the principles of enhanced recovery after surgery (ERAS) pathways (Salamanna et al., 2022).

Technological Interventions: Anti-Gravity Treadmill Training with Virtual Reality

Recognizing that early weight-bearing is not always feasible for all fracture types, recent studies have explored alternative approaches for patients with contraindications to immediate loading. One promising strategy involves the integration of anti-gravity treadmill training with virtual reality, which allows for the simulation of gait and activation of the

sensorimotor system in a safe and controlled environment. The combination of virtual reality and treadmill training significantly enhances walking velocity, stride length, stability and balance confidence in patients with motor impairments, demonstrating superior efficacy compared to treadmill-only training, as evidenced by a systematic review with Level 1A empirical evidence (Hao et al., 2023). Virtual reality offers immersive, tailored environments that enhance patient engagement and motivation in rehabilitation programs (Naqvi et al., 2024; Jeyaraman et al., 2024) and has been shown to facilitate early patient engagement without complications (Hadjipanayi et al., 2024). VR-based interventions have shown promise in improving proprioception, balance and patient engagement for various lower extremity conditions, including total knee arthroplasty, total hip arthroplasty and ACL reconstruction (Wadhokar et al., 2025). The intervention could also help patients manage load distribution more effectively, reducing the cognitive and physical burden associated with crutch use and load monitoring (Galperin et al., 2023). These findings align with broader evidence supporting the use of advanced technologies in orthopedic rehabilitation, particularly in maintaining natural gait patterns and enhancing patient motivation (Paladugu et al., 2025; Atan et al., 2024). However, high costs and the limited availability of such equipment in many clinical settings (Jeyaraman et al., 2024) highlights the importance of developing hybrid rehabilitation models that combine high-tech solutions with more accessible therapeutic options (Mitchell et al., 2023).

Motor Imagery (MI) during Immobilization

Study 3 proposed a rehabilitation intervention during the immobilization period within a cast or brace, incorporating exercises that utilized motor imagery. MI proved to be a valuable tool in the early stages of rehabilitation for conservatively treated patients, as it maintained

neural activation in sensorimotor areas and prevented significant declines in motor function during immobilization. The patients involved appreciated and adopted the proposed intervention, using it independently and significantly reducing the total number of physiotherapy sessions needed to regain normal functionality after the fracture. This suggests enhanced patient self-efficacy (Malouin et al., 2013) and engagement, aligning with literature highlighting MI's capacity to empower patients and reduce healthcare resource utilization (Karakas et al., 2024). The absence of dropouts within the MI cohort further underscored its acceptability, consistent with reports that MI fosters patient empowerment and adherence (Hu et al., 2025). Implementing MI during immobilization could potentially reduce negative effects such as muscle atrophy, reduction in range of motion and diminished cortical representation of the affected limb (Debarnot et al., 2021; Meugnot et al., 2014; Monany et al., 2022). MI is a low-cost, adaptable intervention that requires no specialized equipment or surgical compatibility and its delivery can be easily taught to physiotherapists, enhancing its scalability and clinical utility.

Pain Reduction and Psychological Outcomes

These three studies, despite their distinct focuses and methodologies, collectively support for a paradigm shift in lower limb fracture rehabilitation, moving away from prolonged immobilization towards early, active and tailored interventions.

A key synergistic contribution of this thesis lies in its comprehensive address of the continuum of care. Study 1 demonstrated the safety and efficacy of EWB for suitable fractures, effectively pushing the boundaries of early mobilization. Study 2 offered a possible solution for patients with load restrictions, ensuring early motor practice even when EWB is contraindicated. Study 3 provided a crucial, accessible intervention during the initial phase of

immobilization, before any weight-bearing might be initiated. Together, these studies encompass a broad spectrum of fracture management scenarios, offering complementary strategies for continuous rehabilitation from the point of injury to full recovery.

The research highlights a multimodal approach to recovery. Functional restoration is not merely biomechanical but deeply intertwined with neurological and psychological factors. While EWB primarily emphasizes biomechanical restoration through direct loading, the anti-gravity treadmill combined with VR blends biomechanical simulation with rich neurocognitive engagement. Motor imagery, on the other hand, directly targets neuroplasticity and addresses key psychological barriers such as pain and kinesiophobia. This comprehensive view strongly suggests that optimal rehabilitation necessitates a multi-faceted approach, integrating diverse therapeutic modalities.

The thesis also underscores the balance between technology and accessibility in rehabilitation. Study 2 showcases the transformative power of advanced technology, such as anti-gravity treadmills and virtual reality, in creating protected and engaging rehabilitation environments. Conversely, Study 3 explains the accessibility and cost-effectiveness of a low-tech, cognitive intervention like MI, which can be implemented broadly, even in home settings. This suggests that the ideal future of rehabilitation might involve a blended approach, strategically leveraging high-tech solutions where they offer unique benefits, while universally integrating accessible interventions that address core patient needs and promote self-management.

Another consistent strength across all three studies is the invaluable role of objective biomechanical assessment. The continuous use of motion analysis and GRF measurements provided objective insights into gait adaptations and neuromuscular strategies that extend beyond subjective clinical scales. Even when statistical significance was not uniformly

achieved, the identified trends revealed information about load management, limb symmetry and compensatory behaviors, underscoring the role of these objective tools in understanding complex recovery patterns.

Several overarching insights emerge from these combined findings. A paramount conclusion is the confirmed safety of early intervention strategies; whether through direct loading, simulated movement, or cognitive training, these approaches proved safe, with no observed increase in adverse events. This directly challenges historical paradigms of prolonged immobilization and strongly supports a more proactive approach. Moreover, a consistent emphasis was placed on patient-centered outcomes, particularly independence in ADLs and the ability to return to work and recreational activities. All interventions demonstrated a positive impact on these functional parameters, often leading to clinically meaningful improvements within the crucial first three months post-injury. The underlying rationale for all interventions, from mitigating disuse atrophy to preserving cortical representations and fostering motor relearning, is deeply rooted in the principles of neuroplasticity and sensorimotor control, providing a coherent theoretical framework for the observed benefits across diverse interventions. Importantly, the reduction in pain was a recurring positive outcome across all studies, albeit through different mechanisms and with varying degrees of emphasis. In Study 2, pain scores, measured by the Numerical Rating Scale, showed a steady decline in patients utilizing the anti-gravity treadmill and VR, indicating effective pain management alongside functional gains. However, it was particularly in Study 3, involving motor imagery, that pain intensity was significantly reduced ($p=0.05$), alongside a notable decrease in kinesiophobia ($p=0.0178$). This highlights MI's direct influence on cortical pain modulation circuits and its capacity to mitigate psychological barriers that often impede recovery (Bowering et al., 2014). While Study 1's discussion of pain was less explicit, the observed functional improvements and faster return to daily activities for EWB patients

implicitly suggest better pain management and reduced discomfort over time. This collective evidence underscores the crucial and often underestimated role of psychological factors in recovery; integrating strategies that actively mitigate fear and promote confidence is paramount for achieving optimal rehabilitation outcomes.

Despite their individual contributions, these studies share several common limitations that shape and inform future research endeavors. All studies were constrained by relatively small sample sizes and non-randomized, observational designs, which impacted statistical power, generalizability and the ability to establish definitive causal inferences, often introducing selection and reporting biases. Consequently, future research must prioritize large-scale, multicenter randomized controlled trials (RCTs) with standardized protocols to validate these promising preliminary findings and minimize confounding factors. Furthermore, strict inclusion criteria (healthy, active adults, exclusion of specific comorbidities) and monocentric designs limited the applicability of the results to diverse patient populations, including geriatric, osteoporotic, or polytrauma patients; future studies should actively seek to expand participant diversity to enhance external validity. While providing valuable insights into early and intermediate recovery, the follow-up periods (up to 6 months) do not capture long-term functional sustainability or potential late complications; longitudinal studies with extended follow-up are thus essential to assess the true durability of the observed benefits. From a methodological standpoint, while gait analysis and GRF provided valuable insights, a more comprehensive understanding of neuromuscular adaptation would significantly benefit from quantified EMG data. Additionally, objective measures of motor imagery engagement (e.g., neuroimaging) and musculoskeletal modeling to estimate internal joint forces would provide deeper mechanistic insights. Moreover, the economic impact of these interventions, particularly the more technologically advanced ones, necessitates formal cost-effectiveness analyses to guide healthcare policy and resource allocation, recognizing that low-cost

interventions like MI, widely implementable with minimal equipment, warrant specific evaluation for their scalability and impact in diverse healthcare settings (Dickstein et al., 2007). Finally, future research should explore the utility of wearable sensor technology for ecological assessment of patient activity and biomechanics in real-world settings, thereby overcoming the inherent limitations of laboratory-based assessments.

The thesis evaluated ground reaction forces (GRF) across different patient groups using gait analysis, allowing for the identification of alterations that are often difficult to observe in daily rehabilitation. While movement analysis did not show statistically significant differences between the groups, it revealed subtle but promising trends.

Safety and Complication Rates

Across all involved patients, no increase in adverse events, such as implant failure, nonunion, malunion, loss of reduction, or other postoperative complications, was observed in any patient group. This confirms the safety of these early approaches when applied in appropriately selected populations, aligning with systematic reviews emphasizing the low risk associated with early mobilization protocols (Canton et al., 2022; Aprisunadi et al., 2023; Sharma et al., 2022).

Critical Interpretation of Results

The findings of this research provide important insights into the multifactorial nature of functional recovery following lower limb fractures and the potential mechanisms through which early and innovative rehabilitation strategies exert their effects. Clinically, the observed acceleration in functional autonomy and reduction in pain and kinesiophobia among patients

receiving MI interventions suggest that these cognitive-motor approaches engage neurophysiological pathways beyond mere musculoskeletal repair.

From a physiological perspective, the benefits of MI can be interpreted through the lens of neuroplasticity. MI activates neural circuits overlapping with those involved in actual movement execution, including the primary motor cortex, premotor areas, supplementary motor area, basal ganglia and cerebellum (Hanakawa et al., 2003; Lotze & Halsband, 2006). This activation likely preserves cortical representations of the affected limb during immobilization, mitigating the deleterious effects of disuse such as muscle atrophy, cortical thinning and decreased corticospinal excitability (Debarnot et al., 2021). Despite ongoing debate in the scientific community regarding neuroplasticity, a confirmed need remains to focus on maintaining and optimizing existing neural and functional structures through appropriate training and stimulation. The use of cognitive strategies during the acute phase, when the limb cannot perform its normal functions, could help reduce recovery times by maintaining the normal activation of involved neural circuits, rather than relying on a subsequent period for potential reorganization.

The reduction in pain and fear of movement observed in the MI group aligns with the biopsychosocial model of pain. MI may modulate pain perception by engaging descending inhibitory pathways and altering maladaptive cortical activity patterns. The reciprocal relationship between pain intensity and kinesiophobia supports previous findings that early psychological interventions can prevent chronic disability.

Biomechanically, the improved GRF symmetry and variability in the MI group suggest enhanced sensorimotor integration and postural control, despite immobilization. This is consistent with the concept that MI facilitates the maintenance of interlimb coordination and motor planning. The tendency of control patients to shift their COM toward the contralateral

limb reflects common compensatory strategies post-injury, which may predispose to secondary musculoskeletal problems and delayed functional recovery.

The integration of anti-gravity treadmill training and virtual reality in Study 2 further exemplifies the importance of multisensory and task-specific stimulation in rehabilitation. These technologies provide graded mechanical loading and enriched sensorimotor feedback, promoting cortical reorganization and motor relearning. However, their limited accessibility highlights the value of MI as a scalable alternative that can engage similar neural circuits without reliance on costly equipment. Overall, these results support a neurocognitive framework for fracture rehabilitation, wherein early engagement of sensorimotor networks through cognitive and physical means can preserve neural function, reduce maladaptive plasticity and optimize clinical outcomes. This perspective aligns with emerging paradigms in neurorehabilitation emphasizing the central nervous system's role in musculoskeletal recovery.

Strengths and Limitations

The studies collectively employed a rigorous and unified methodological approach, characterized by consistent inclusion and exclusion criteria. The targeted exclusion of patients with cognitive problems ensured the internal validity of the study, preventing potential bias stemming from the inability to accurately follow physiotherapy instructions. The use of standardized outcome measures across all three observational studies enhances the comparability of findings. The experimental design incorporated rigorous, objective assessment tools, including advanced stereophotogrammetric systems for gait analysis and force platforms for GRF measurements. This multimodal approach, along with sophisticated data processing, allowed for comprehensive analysis essential for understanding rehabilitation effects. The use of validated clinical scales ensured comparability with existing literature.

Furthermore, this study is among the first to analyze GRF and motor control-related tasks like gait initiation in this patient population during early recovery, providing novel insights.

Despite these strengths, several limitations must be acknowledged. Each study included a relatively small sample size (no more than 20 patients per group), which limits statistical power and generalizability. The monocentric design further constrains external validity. The follow-up periods (6 weeks, 3 and 6 months) provided insights into early and intermediate recovery but did not capture long-term functional outcomes or potential late complications. Technical and methodological limitations also affected reproducibility and interpretation. Individualized surgical decisions regarding weight-bearing introduced variability. The use of specialized equipment limits scalability. While joint range of motion was assessed, the use of a long-arm goniometer, though standard, is operator-dependent and more precise devices could have improved accuracy. Additionally, a formal quantitative analysis of surface electromyography (EMG) data was not performed, representing a limitation as precise quantification of muscle activity would have provided critical insights into neuromuscular adaptations. While GRF analysis offers objective biomechanical data, it does not fully capture internal joint loading or muscle co-contraction patterns.

Furthermore, the assessment conducted in a laboratory setting inherently makes the movement less ecological, requiring patients to focus more on the task at hand. This limits understanding of how patients maintain GRF symmetry control in different conditions. The fact that gait analyses were conducted at self-selected walking speeds, which were notably slow due to patient-perceived pain and fear of movement, also limits generalizability, as gait biomechanics are highly speed-dependent (Fukuchi et al., 2019).

Clinical Implications

The results of this research have important implications for clinical practice and rehabilitation protocols in the management of lower limb fractures. Early rehabilitation interventions, such as early weight-bearing, MI and anti-gravity treadmill training with virtual reality, offer promising avenues to enhance recovery while addressing challenges of immobilization.

From a clinical standpoint, the confirmation of safety and efficacy of early weight-bearing supports its integration into postoperative protocols for selected patients, aligning with trends toward accelerated rehabilitation and ERAS pathways. This approach can shorten disability duration and reduce immobilization-related complications. The use of MI during immobilization presents a low-cost, accessible strategy for diverse clinical settings. By preserving neural representations of movement and reducing pain and kinesiophobia, MI can facilitate earlier engagement in active rehabilitation and potentially decrease supervised physiotherapy sessions. This empowerment of patients to self-manage aligns with patient-centered care principles and may improve adherence and satisfaction. Anti-gravity treadmill training combined with virtual reality offers an advanced option for safe, graded loading and enriched sensorimotor feedback, critical for neuromotor re-education.

These findings advocate for a more flexible and individualized approach to rehabilitation protocols, considering patient-specific factors such as fracture complexity, surgical stability, psychological readiness and resource availability. Incorporating objective assessments like gait analysis and validated functional scales can guide clinicians in tailoring interventions and monitoring progress. Early identification and management of psychological barriers, including kinesiophobia, are essential to optimize outcomes. Overall, integrating cognitive and physical rehabilitation strategies informed by neuroplasticity principles can

transform traditional fracture care from a passive, impairment-focused model to an active, patient-engaged process. This shift has the potential to improve efficiency, reduce healthcare costs and ultimately enhance patient recovery trajectories.

Future Directions

To build on these preliminary findings, future research should prioritize multicenter, randomized controlled trials with larger sample sizes to enhance statistical robustness and external validity. Such studies would enable subgroup analyses and stratification based on fracture type, patient demographics and psychological factors. A particular emphasis should be placed on psychological constructs like kinesiophobia, aiming to identify risk and predisposing factors for fear of movement, enabling early targeted interventions.

The integration of emerging technologies offers exciting possibilities. Combining MI with virtual reality, biofeedback and wearable sensor systems could enhance patient engagement, provide real-time feedback and enable remote monitoring. Neuroimaging modalities such as fMRI and MEG could elucidate the neural mechanisms underlying rehabilitation-induced plasticity, providing biomarkers for recovery and guiding personalized treatment (Burianova et al., 2016). Musculoskeletal modeling could also be included to better estimate joint contact forces, as GRF alone does not fully represent joint loading. Kinetic data transforms gait analysis from observational to mechanistic, enabling clinicians to address root causes of impairment.

Cost-effectiveness analyses are also essential, particularly for expensive technologies like anti-gravity treadmills. Low-cost interventions such as MI, which can be widely implemented with minimal equipment, should be evaluated for their scalability and impact in

diverse healthcare settings (Dickstein et al., 2007). Finally, the possibility of expanding subject groups with the same fracture types and interventions could provide greater statistical evidence.

Final Conclusions

This thesis advances the understanding of rehabilitation after lower limb fractures by demonstrating that early, individualized and neurocognitively informed interventions can significantly improve recovery outcomes. Early weight-bearing, anti-gravity treadmill training combined with virtual reality and motor imagery each offer unique benefits that, when appropriately applied, can accelerate functional restoration, reduce pain and mitigate psychological barriers such as kinesiophobia.

The original contribution of this work lies in its integrative approach, combining biomechanical, neurocognitive and psychological perspectives to inform precision rehabilitation. Motor imagery emerges as a particularly accessible and scalable strategy, capable of preserving motor representations and facilitating recovery even during immobilization phases. Ultimately, this research supports a paradigm shift in fracture rehabilitation, moving from passive, impairment-focused care to proactive, patient-centered strategies that harness neuroplasticity and sensorimotor engagement. Such an approach promises to optimize clinical outcomes, reduce healthcare burdens and empower patients throughout their recovery journey, laying the groundwork for future innovations in orthopedic rehabilitation.

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