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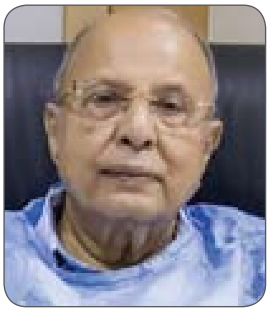

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President's Message

Dr. Sushrut Babhulkar

Dear Readers and Esteemed Fellow Colleagues,

It is with great honour and a deep sense of responsibility that I address you in the inaugural edition of the Journal on Trauma, a pioneering initiative in India dedicated to exploring and addressing the multifaceted dimensions of orthopedic trauma.

In a world that is rapidly evolving, the impact of trauma—whether it stems from conflict, natural disasters, personal loss, or systemic injustice—remains a profound and pervasive challenge. The journey towards healing and resilience begins with understanding of various fractures , its treatment algorithms, newer thought processes, and this journal represents a vital step in that journey towards spread of knowledge.

Orthopedic trauma both for the patient and to the operating surgeon, is not just an individual experience but a collective one that shapes our communities, institutions, and nations. Its effects can be far-reaching, influencing mental health, social structures, and the very fabric of society. As we embark on this ground-breaking endeavour, it is crucial to acknowledge the diverse contexts in which trauma manifests and to approach it with compassion, scientific rigor, and a commitment to positive change. We hope to bring to you the latest in the management of fracture fixation. We will not only discuss the current thoughts but also look at evidence based global literature.

I encourage each of you to engage with this publication not only as a source of information but as a catalyst for meaningful conversation and collaboration. Together, let us work towards a future where the impacts of orthopedic trauma related fracture fixation methodologies are understood, addressed, and transformed into opportunities for growth and fracture healing.

As we launch this inaugural issue at the Traumacon 2024 in India, let us be guided by the principles of empathy, respect, and a shared commitment to improving the lives of those affected by trauma. I look forward to witnessing the positive contributions this journal will make to our collective understanding and response to trauma in India and beyond.

Thank you for your dedication to this important cause.

With sincere regards,

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Review article

Intra-articular Fractures of the Distal Radius Treated via Dorsal Approach: A Narrative Review

Dr Nitin Kimmatkar*, Dr Ashok Gavaskar**, Dr Amol Dubepuria ***#

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Abstract

Distal radius fractures are common injuries, accounting for a significant portion of emergency room cases, and affecting both young adults and the geriatric population. High-energy trauma usually causes intra-articular fractures in younger individuals, while older adults often suffer from extra-articular fractures. Treatment aims at anatomic reduction and stable fixation to restore function, with options including closed reduction and casting, percutaneous fixation, external fixation, and open reduction internal fixation (ORIF) via dorsal or volar approaches.

The dorsal approach offers advantages like direct visualization of fracture fragments and support against dorsal collapse, making it ideal for complex fractures with dorsal comminution. Comparative studies show similar clinical and radiological outcomes between dorsal and volar plating, though each approach has associated complications. The introduction of low-profile locking plates has decreased tendon irritation associated with dorsal plating, increasing its effectiveness for certain fracture patterns. Although some research suggests a greater likelihood of implant removal with dorsal plating, both methods are effective in restoring wrist function. Further high-quality studies are needed to determine the best surgical approach for various types of distal radius fracture.

Distal radius fractures – An overview

Distal radius fractures (DRFs) are among the most frequently encountered fractures in emergency room accounting for one-sixth of all fractures seen, affecting both the young and the elderly [1]. The presence of an intra-articular component in DRFs usually indicates high-energy trauma, commonly observed in young adults. Such injuries often cause shear and impacted fractures of the articular surface at the distal end of the radius, resulting in displaced fracture fragments. Conversely, extra-articular fractures are more frequent in the elderly, whereas high-energy intra-articular fractures are more common in younger adults [2]. There might be a need for different treatment approaches due to variations in bone quality, fracture characteristics, associated soft tissue injuries and patient's functional demand between these age groups [3].

Prevalence of distal radius fractures

The DRFs account for 17.5% of all fractures in adults. Factors contributing to the rising rates of DRFs include lifestyle, increased life expectancy, increased travelling, childhood obesity, and higher osteoporosis rates in the elderly. Studies have shown that DRFs primarily affect young males and postmenopausal females [4].

Pathophysiology of distal radius fractures

“Distal radial fracture” is a broad term for any radius fracture near the wrist, but the various types can differ in presentation, mechanism of injury, and its management. Familiarity with the specifics of each type is key to appropriate treatment (Table 1) [5].

Treatment options

The primary goal of fracture treatment is to achieve accurate reduction of the fracture fragments, followed by maintaining this reduction by application of an immobilization method. Although restoring normal function is the ultimate objective in managing DRF, the best approaches to achieve this remains a topic of debate. It might be particularly challenging to treat intra-articular fractures of the distal radius using traditional conservative methods. Therefore, a variety of treatment options are available to prevent loss of reduction in unstable DRFs, each offering distinct benefits and considerations [2].

Closed reduction and casting

Treatment of DRF mainly involves closed reduction and immobilization in a splint or cast, which has been the standard for nondisplaced and stable fractures. Closed reduction is typically performed under various forms of anesthesia, including procedural sedation, hematoma block, regional nerve block, intravenous regional anesthesia, or general anesthesia. Each sedation method has its own risk of complications, and due to limited literature, no single method is universally recommended [6].

Fractures exhibiting minor comminution and minimal or no displacement are generally suitable for closed reduction and cast immobilization. Specifically, type I Melone’s fractures can typically be managed conservatively [2].

Percutaneous fixation

Multiple authors have described the use of Kirschner wires for minimally invasive stabilization of extra-articular fractures [6]. Glickel et al. found that closed reduction and percutaneous pinning for DRFs led to excellent long-term outcomes, with all fractures healing within 6 weeks. There were minimal differences in range of motion and grip strength compared to the uninjured wrist, supporting this as an effective, low-cost treatment for two- and three-part fractures [7].

A Cochrane meta-analysis of 13 clinical trials on percutaneous pinning for DRFs found limited evidence for its effectiveness and noted high complication rates, especially with Kapandji fixation and biodegradable pins. Although percutaneous pinning may improve anatomical outcomes compared to plaster casts, its exact role and methods are still uncertain [8].

External fixation

External fixation is regarded as a superior treatment option compared to plaster immobilization for patients with intra-articular comminuted DRFs. Other indications for external fixation include [2]:

- Unstable extra-articular fractures with significant comminution
- Associated comorbidities

Table 1. Common distal radius and forearm fractures: Mechanisms, characteristics and X-ray appearance

Fracture Type	Mechanism of Injury	Characteristic Features	X-Ray Appearance
Colles’ Fracture	FOOSH	Metaphyseal fracture ~1.5 inches proximal to carpal articulation; dorsal angulation and displacement	“Dinner-fork” deformity
Smith’s Fracture	Fall onto dorsum of hand or direct blow	Volar angulation of distal fragment; reverse Colles’	“Garden-spade” deformity
Chauffeur’s Fracture	FOOSH with wrist blow	Intra-articular fracture of the radial styloid; variable fragment size	Variable, intra-articular
Die-Punch Fracture	Axial loading of lunate	Intra-articular fracture involving lunate facet of radius	Lunate facet impaction
Galeazzi Fracture-Dislocation	FOOSH	DRUJ dislocation	Radius fracture, DRUJ disruption
Barton’s Fracture	Forced dorsiflexion/ pronation or fall	Intra-articular rim fracture of distal radius; classified as dorsal or volar	Avulsed fragment displacement
Greenstick Fracture	Bending forces	Incomplete fracture; convex surface fracture with intact concave surface	Bony bending
Buckle/Torus Fracture	Axial loading	Incomplete fracture; buckling of bony cortex and periosteum without true fracture lines	Buckled cortex and periosteum
Salter-Harris Fracture	Various	Fractures involving epiphyseal plate, classified I-IX	Varies by type

FOOSH: Fall On an Outstretched Hand; DRUJ: Distal Radioulnar Joint

- Presence of significant swelling
- Severe open fractures with substantial soft tissue damage and neurovascular compromise

External fixation utilizes the principle of ligamentotaxis to apply traction and restore alignment. It is considered the most effective way to overcome the muscle forces that can cause collapse of comminuted DRFs. Recent studies have provided increasing support for the use of external fixation in managing unstable intra-articular DRFs, demonstrating its effectiveness in achieving stable fixation and facilitating recovery [2].

Egol, et al conducted a prospective randomized study comparing bridging external fixation with supplemental Kirschner wire fixation to volar locked plating for unstable DRFs. The researchers found that both treatment methods resulted in similar functional outcomes and complication rates [9].

Open reduction internal fixation

Dorsal

Internal fixation of DRFs is typically used for significant dorsal comminution or displacement. However, high rates of tendon irritation and extensor pollicis longus ruptures have made dorsal plating less favorable, necessitating routine removal of these plates to avoid complications. As a result, virtually all dorsal bridge plates warrant routine removal to avoid tendon complications. Dorsal plating is now primarily reserved for fractures with severe dorsal comminution that cannot be stabilized with volar plating [6].

Volar

Internal fixation for DRFs has gained significant attention since the introduction of volar locking plate in the early 2000s. Numerous studies support the effectiveness of internal fixation, despite concerns about the higher costs. Volar plates are believed to be superior to dorsal plates due to their more biologically friendly approach to extrinsic tendons and better preservation of the metaphyseal blood supply. However, drawbacks of volar fixation include the risk of flexor pollicis longus tendon irritation and subsequent rupture due to plate prominence, potential intra-articular screw penetration, and irritation of the extensor tendons from prominent screws in the dorsal cortex. Retrospective and comparative studies have shown that volar plate fixation is successful in treating unstable DRFs, reinforcing its position as a reliable treatment option [6].

Rozental et al. conducted a study comparing open reduction and internal fixation using a volar plate with percutaneous fixation for treating dorsally displaced unstable DRFs. The results indicated that the volar plate group had significantly better early functional recovery, as measured by Disabilities of the Arm, Shoulder and Hand scores, making it the preferred method for patients requiring a faster return to function [10].

Similarly, Karantana et al. compared outcomes of displaced distal radial fractures treated with a volar locking plate versus conventional closed reduction and percutaneous fixation in 130 patients. While the volar locking plate group showed better early functional outcomes and grip strength, no significant long-term differences were observed, suggesting it facilitates quicker initial recovery but does not provide lasting functional advantages over conventional treatment [11]. Recent American Academy of Orthopaedic Surgeons (AAOS) guidelines found insufficient evidence to make definitive recommendations for or against any treatment method. Despite the growing popularity of volar locking plate fixation, there is a lack of high-quality studies comparing it to other treatment options [6].

Fragment-specific fixation

Fragment-specific fixation employs a combination of low-profile small plates and clips that can be tailored to the specific fracture pattern and fragments involved. This method allows for internal fixation in highly comminuted fractures where standard plating is challenging, thus avoiding external fixation. Although technically demanding and time-consuming, requiring experienced surgeons and often multiple incisions, it offers a customized solution for complex fractures [6].

Dodds et al. compared the biomechanical stability of fragment-specific fixation and augmented external fixation for intra-articular DRFs. The findings showed that fragment-specific fixation offered comparable stability for 3-part fractures and significantly greater stability for 4-part fractures, supporting its use for early wrist motion in treating complex fractures [12].

Clinical overview of dorsal approach for partial articular fracture of the distal radius

Rikli and Regazzoni proposed a “3-column” theory to describe the anatomy of DRFs, categorizing the distal forearm into three distinct columns: the radial or lateral, intermediate, and ulnar or medial. In the “3-column” theory, the radial column includes the radial styloid and scaphoid fossa, the central column consists of the ulnar portion of the distal radius, sigmoid notch, and lunate facet, while the ulnar column is made up of the distal ulna, ulnar head, and triangular fibrocartilage complex [13, 14].

The primary aim of surgical treatment for DRFs is to achieve anatomical reduction and restore the three columns of the distal radius - the radial column, central column, and ulnar column. Restoring the anatomy is crucial to minimize the risk of post-traumatic arthritis. Surgical techniques that provide optimal exposure and visualization of the distal radius are essential to maximize the chances of achieving anatomical reduction of the fracture fragments [14].

The choice between dorsal and volar plating for DRFs is influenced by factors such as fracture type, location, direction of fragment displacement, and surgeon preference. Dorsal plating offers advantages like direct visualization of fracture fragments and the ability to provide support against dorsal collapse. Techniques utilizing dorsal plating are often considered ideal for treating complex fractures. Several studies have demonstrated the effectiveness and positive clinical

Table 2: Clinical overview of dorsal approach for DRFs

Study	Patients	Follow up	Results			Conclusion
Smet, et al [16]	26 patients with intra-articular impacted fractures	39 months	VAS	1-4 (46%); ≥5 (23%)		The dorsal approach is a viable treatment for certain intra-articular fractures, providing direct control of intra-articular congruency and stable buttress locking fixation, which facilitates early mobilization.
			QuickDASH Score	20±10.77		
			Mayo Wrist Score	70±18.49		
			SANE Score	76%±18.95		
			Flexion-Extension Range of Motion	92° ± 30.79		
			Wrist Flexion	37°±18.12		
			Wrist Extension	54±17.34		
			Ulnar Deviation	23°±8.73		
			Radial Deviation	15°±11.66		
			Supination	82°±11.48		
			Pronation	77°±13.73		
			Grip Strength	29 kg±12.65		
Abe, et al [17]	112 patients with displaced intra-articular fractures who were treated with dorsal (n=38) or volar approach (n=68)	Dorsal plate (13±5.5); Volar plate (12.6±5.5)	• Clinical Results: No statistical differences in subjective and objective parameters, except for wrist flexion. • Complication Rates: No significant differences between volar and dorsal plated groups. • Serious Complications: One serious complication occurred after volar plating. • Reason for Dorsal Plating: Most common reason was irreducible dorsal die-punch fractures.			Dorsal and volar interlocking plates for displaced intra-articular DRFs yielded similar clinical outcomes, with no significant postoperative complications in the dorsal group.
Nasab, et al [18]	70 adult patients with closed fracture in proximal half of the radius or radius and ulna who were treated with dorsal (n=31) or volar approach (n=39)	16 weeks	Parameter	Volar Approach	Dorsal Approach	There was no significant difference in term of fracture union, early complications, and range of forearm rotation between volar and dorsal approach for the fixation of radius fractures in its proximal half.
			Radial Nerve Injury	3 patients	2 patients	
			Infection	1 patient	1 patient	
			Nonunion	1 patient	1 patient	
			Duration of Procedure	No significant difference	No significant difference	
			Mean Forearm Rotation (4 months)	135°	138°	
Wei, et al [19]	Quantitative meta-analysis of 12 trials (952 patients)		• No between-group difference in overall complication rate • Volar fixation » Increased neuropathy (RR 2.19; 95% CI 1.27, 3.76) » Increased carpal tunnel syndrome (RR 4.56; 95% CI 1.02, 20.44) » Reduced tendon irritation (RR 0.38; 95% CI 0.17, 0.86)			Dorsal fixation has a lower risk of neuropathy and carpal tunnel syndrome than the volar approach but a higher risk of tendon irritation.

Drummond, et al [20]	394 patients with DRFs treated with dorsal bridge plating (DBP) or volar plate fixation)	55.2 weeks	DASH score	25.7	
			Range of Movement	46.9° flexion, 48.8° extension, 68.4° pronation, 67.5° supination	DBP is a good alternative to volar plating for complex DRFs with satisfactory outcomes.
			Radiological Parameters	Radial Height: 10mm, Volar Tilt: 3.1°, Ulnar Variance: 0.5mm, Radial Inclination: 18.8°	
			Complication Rate	11.4% (Digital stiffness most common, improved with tenolysis)	
Abbreviations - VAS: Visual Analog Scale; QuickDASH: Quick Disabilities of the Arm, Shoulder, and Hand; SANE: Single Assessment Numerical Evaluation; RR: Relative Risk; CI: Confidence Interval; N/A: Not Applicable					

outcomes associated with the dorsal approach for partial articular fractures of the distal radius (Table 2) [14, 15].

A case study presented a 60-year-old woman with a dorsally unstable, displaced intra-articular DRF treated via a dorsal approach. At one-year post-surgery, the patient achieved near full and painless range of motion in her wrist, with no significant complications or post-traumatic arthritis observed on radiographs. The study emphasizes that the dorsal approach provides reliable restoration of wrist function with a lower rate of neuropathic complications compared to other methods [15].

The existing research comparing dorsal and volar plating techniques for DRFs shows varying results in terms of complications. While some studies suggest a higher incidence of implant removal with the dorsal approach, the overall radiographic and clinical outcomes appear to be similar between the two methods. The introduction of newer, lower-profile locking plates has helped reduce certain complications associated with dorsal plating, potentially making it a suitable option for managing specific fracture patterns. However, more high-quality comparative studies are needed to definitively determine the optimal surgical approach for different types of DRFs [15].

Conclusion

The treatment of DRFs, particularly those involving intra-articular components, remains a complex and debated topic in orthopedic surgery. The dorsal approach for partial articular fractures of the distal radius offers distinct advantages such as direct visualization of fracture fragments and support against dorsal collapse, making it a valuable option in specific fracture patterns. Despite the higher complication rates associated with dorsal plating, advancements in low-profile locking plates have reduced these risks, providing comparable outcomes to volar plating in many cases. However, a surgeon should not hesitate in using combination of dorsal and volar approach in complex fracture patterns for anatomic reduction. Continued research and high-quality comparative studies are needed to improve treatment protocols and optimize patient outcomes, ensuring tailored approaches based on fracture characteristics and patient-specific factors.

Article information

Conflicts of interest

The authors has no conflict of interest to declare.

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Data availability

Data of this study are available from the author/s upon reasonable request

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Review article

Open Tibial Shaft Fracture Fixation Strategies: Intramedullary Nailing, External Fixation and Plating

Dr Yogesh Salphale*, Dr Wasudeo Gadegone**, Dr Sumedh Chaudhary***#

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Abstract

Tibial shaft fractures are among the most prevalent orthopedic injuries, representing about 2% of all fractures in adults and 37% of long bone fractures. These injuries occur frequently in both high-energy trauma scenarios and low-energy falls, with significant variations in treatment based on fracture severity and patient age. The Gustilo-Anderson classification guides treatment based on fracture severity. Conservative treatment with casting is effective for stable fractures but carries risks like delayed union and malunion. Surgical management, including external fixation, intramedullary nailing (IMN), and plating, is essential for displaced or complex fractures. External fixation offers rapid stabilization but has higher infection risks. IMN, preferred for its stability and minimal soft tissue damage, is effective for diaphyseal and open fractures. Plating is less common but useful for specific fracture patterns. Management of tibial shaft fractures requires a tailored approach considering fracture type, patient health, and potential complications. Both conservative and surgical methods have specific advantages and limitations. Further studies are needed to optimize treatment strategies and improve patient recovery.

Keywords: Tibial shaft fractures, Open tibial fractures, External fixation; Intramedullary nailing; Percutaneous locking plate

Tibial shaft fractures – An overview

Tibial shaft fractures are among the most common long bone fractures, often resulting from high-energy injuries such as motor vehicle accidents, which account for approximately 43% of cases. The overall incidence is estimated to be between 17 and 21 per 100,000 individuals, with open tibial fractures account for approximately 25% of all leg shaft fractures. These fractures are particularly concerning due to their potential to cause long-term complications, prolonged hospital stays, and increased healthcare costs. High-energy trauma, such as falls from significant heights and motor vehicle accidents are the most common causes of tibial shaft fractures. Research indicates a bimodal distribution in the presentation of these fractures, where younger individuals typically experience them following high-energy events. At the same time, older adults often sustain fractures from lower-energy incidents, such as ground-level falls. The added complexity of soft tissue involvement makes it especially difficult to treat open tibial shaft fractures. Open tibial shaft fractures are complicated because of the added complexity of soft tissue involvement. Effective fracture fixation strategies are crucial to reduce the risk of complications such as malunion, nonunion, infection or other postoperative complications [1,2,3].

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Classification of tibial shaft fractures

The severity of an open fracture significantly affects both the treatment approach and patient outcomes. This has led to the establishment of grading systems that systematically categorize fractures with similar characteristics. The Gustilo-Anderson classification system, known for its simplicity and practicality, has been widely utilized for all types of open fractures for the last 36 years, even though it was initially developed specifically for tibial fractures (Table 1) [4,5].

Table 1. Gustilo-Anderson classification for open tibia fractures

Type	Description	Wound Characteristics
Type I	Limited periosteal stripping	Clean wound less than 1 cm
Type II	Mild to moderate periosteal stripping	Wound greater than 1 cm in length
Type IIIA	Significant soft tissue injury, significant periosteal stripping	Wound greater than 1 cm in length, no flap required
Type IIIB	Significant periosteal stripping and soft tissue injury	Flap required due to inadequate soft tissue coverage
Type IIIC	Significant soft tissue injury with a vascular injury	Vascular injury requiring repair

Etiology

High-energy traumas, particularly motor vehicle collisions, are the predominant cause of proximal tibial fractures in men. In contrast, most fractures in women result from low-energy mechanisms, such as falls during walking or cycling. Typically, low-energy injuries result in unilateral depression-type fractures, whereas high-energy injuries can lead to comminuted fractures that involve significant damage to bone, soft tissue, and neurovascular structures. Fractures of the tibial head can occur due to forces acting from multiple directions, including medial, lateral, or axial forces. Medial forces, often referred to as valgus forces, are commonly associated with “bumper fractures,” which occur in pedestrian accidents involving vehicles. More intricate injury mechanisms may involve a combination of axial forces along with varus or valgus forces. In many cases, both shearing and compressive forces affect the tibial plateau through the femoral condyle, impacting it from either the medial or lateral sides [6].

Conservative treatments

Stable, non-displaced fractures of the tibial shaft can be effectively treated with conservative methods, typically involving the application of a cast. This conservative approach usually involves wearing a thigh plaster cast for about 4 weeks, after which a functional brace may be utilized for an additional 8 to 12 weeks. There is no clear consensus on the acceptable limits for articular step-off and gaps; however, discrepancies of less than 2 mm and gaps of under 5 mm are generally regarded as tolerable [6,7].

Regular radiographic monitoring is essential, typically performed every 2 weeks. The duration of treatment depends on the fracture type, with rotational fractures generally requiring 8-10 weeks and transverse fractures needing at least 12 weeks of immobilization. However, the extended period of cast treatment increases the risk of deep venous thrombosis, compartment syndrome, soft tissue injury, and chronic regional pain syndrome. Casting for tibial fractures is associated with the lowest incidence of infection; however, it has a higher prevalence of delayed union, nonunion, and malunion. Furthermore, diagnosing soft tissue injuries and compartment syndrome is more difficult when the fracture is managed with a cast [7].

Principles of surgical management

Historically, open fractures have been associated with high mortality rates and severe outcomes. However, advancements in modern surgical techniques have dramatically improved the prognosis for these injuries. Standard principles in managing open fractures include:

- Initial assessment and resuscitation
- Antibiotic and tetanus prophylaxis
- Surgical debridement and copious irrigation
- Fracture stabilization
- Soft tissue closure
- Thorough rehabilitation
- Adequate follow-up

Additionally, surgeons can utilize adjunct therapies such as local antibiotic therapy, vacuum-assisted therapy, free tissue transfer, or bone grafting. The primary goals are to prevent infection, promote healing, and restore function. However, if necessary, a delayed primary amputation should be considered within 72 hours of the injury [4].

Surgical treatments

Surgery may be indicated for open fractures, fractures that fail to heal with non-surgical methods, fractures with displacement, or those with multiple fragments. Operative treatment using standardized protocols is frequently employed. Prolonged casting can lead to significant discomfort for patients and may present challenges in managing the fracture effectively. Immediate surgical intervention is necessary in cases such as open fractures, compartment syndrome, concurrent nerve or vessel injuries, or when multiple injuries are present. Definitive skeletal stabilization should be performed as soon as possible after debridement; if this is not feasible, temporary external fixation is recommended. Surgical techniques for bone fixation include intramedullary nailing (IMN), external fixation, and plate-and-screw fixation. The choice of technique should be based on the fracture's location, type, and the extent of soft tissue damage [4,7,8].

External fixation

External fixation involves realigning the fractured bone fragments, typically through closed reduction, and/or transverse insertion of ~~metal~~ screws and pins into the bone segments above and below the fracture site. These screws/pins are then attached to a stabilizing bar structure that remains outside the skin. This technique allows the bones to be held in the correct position to facilitate healing [8].

Beltsios et al. conducted a retrospective study to assess the effectiveness of unilateral external fixators for treating open tibial fractures, severe soft tissue injuries, threatened compartment syndrome, and multiple injuries. The study included 223 patients, with 139 having Gustilo Type III open fractures. The average time to fracture union was 25 weeks. Complications included 18 nonunions, 21 delayed unions, 4 malunions, 58 pin site infections, and 3 cases of osteomyelitis. The authors concluded that advancements in external fixator technology make them a viable option for severe tibial shaft fractures, especially with significant soft tissue damage or impending compartment syndrome [9].

Indications

External fixation is recommended as the primary method of stabilization for patients with multiple traumas, severe soft tissue injuries near joints, or those who are generally not suitable for surgical intervention. There are no contraindications for using external fixation in cases of tibial shaft fractures. According to the damage control principle, initial external fixation is the preferred approach for managing multiple trauma patients. Additionally, patients at higher risk include those with thoracic injuries, craniocervical trauma, hypothermia, or coagulopathy. The risk of infection does not increase if a procedural change is made within 5 to 10 days. Primary external fixation is also beneficial for severe soft tissue injuries without fractures, as it provides necessary immobilization. Furthermore, external fixators continue to be employed for the definitive treatment of juvenile tibial shaft fractures [7].

Outcomes

While external fixators allow for quick fracture stabilization and minimize further soft tissue damage, when used as the definitive treatment they frequently lead to complications such as pin loosening, pin tract infections, and malunion. Infection of the tissue around the pin sites is a common complication of external fixation, which can be mitigated by using proper pin insertion technique and meticulous postoperative pin site care. Although these infections are typically localized and rarely progress to osteomyelitis, intramedullary nails should be used judiciously if an infection develops at the pin site [7,8].

Intramedullary nailing (IMN)

IMN is currently the most widely used method for treating tibial fractures, although there are specific indications and contraindications. The procedure involves the insertion of a specialized metal rod (typically made of titanium) into the tibial canal after a closed or open reduction of the bone fragments. The intramedullary rod is secured to the bone at both ends, ensuring that the nail and bone remain properly aligned throughout the healing process. The key advantages of IMN include biomechanical stability, a minimally invasive approach that avoids direct exposure to the fracture site, preservation of the periosteal blood supply, limited soft tissue damage, and the ability to control alignment, rotation, and translation. Evidence strongly supports the use of IMN as the preferred implant for diaphyseal tibial fractures. Additionally, substantial evidence indicates that intramedullary nails provide advantages over external fixation for open fractures, provided that wound closure can be achieved shortly after initial stabilization [1,7,8].

Indications

IMN is indicated for open and closed isolated tibia shaft fractures, extraarticular distal tibial fractures, oblique, transverse, segmental, torsion, debris fractures, and open fractures with bone loss. It is also used for segmental, comminuted, bilateral tibia fractures, and ipsilateral limb injuries. IMN is contraindicated in cases of severe soft tissue injuries, multiple trauma patients, thoracic trauma, infection, non-union, or children with joint growth. In open tibia fractures, IMN can be effective within 24 hours. It is also contraindicated in children with open physis, where, external fixation is preferred. Recent advancements in nail design and reduction techniques have expanded IMN indications to include proximal and distal third tibial fractures [7,8].

Outcomes

IMN is considered a standard treatment for diaphyseal fractures of long bones, despite risks such as endosteal necrosis and systemic fat embolism. It supports biological osteosynthesis by preserving the fracture hematoma. The use of angular stable locking screws enhances control over rotation, length, and alignment, expanding its indications. However, there is an ongoing debate about whether IMN should be performed with reaming or unreamed, and whether to use locking screws [7].

Intramedullary reaming deposits debris at the fracture site, acting as an autologous bone graft and enhancing cortical contact for better stability. However, it can disrupt the endosteal blood supply, which is crucial for healing. In contrast, unreamed IMN preserves this blood supply, leading to faster healing and a lower risk of infection. Due to the negative effects of reaming on the endosteal blood supply, unreamed IMN has become widely used for both open and closed tibial shaft fractures. This technique is preferred for its ability to maintain the endosteal blood supply, thus reducing complications associated with healing. Consequently, unreamed IMN has seen extensive clinical use for both open and closed tibial shaft fractures [7].

Tielinen et al. conducted a study to evaluate the outcomes of acute surgical debridement, unreamed IMN, and muscle flap reconstruction for severe Gustilo type IIIB to IIIC open tibial shaft fractures. Over a 10-year period, 19 patients with extensive soft tissue injury and suitable for nailing were treated. Follow-up assessments showed all fractures healed without infection complications, with a mean union time of 8 months. A total of nine patients experienced delayed healing, requiring additional interventions such as exchange nailing or bone grafting. The overall functional outcome was good in 18 of 19 patients despite some tibial shortening and external rotation in a few cases. The study concluded that acute surgical debridement, unreamed IMN, and muscle flap reconstruction are safe and effective for treating severe open tibial shaft fractures [10].

Percutaneous locking plate

Plating, also known as plate osteosynthesis, is a less common method for fixing open tibial shaft fractures. The process begins with repositioning the fractured bone fragments through either closed or open reduction techniques. Initially, an incision is then made on the skin to access the bone, and plates are applied through this incision. These plates are secured to the bone with screws, which hold the bone segments together and promote healing [1,8].

Indications

Traditionally, conventional plate osteosynthesis was the preferred method for tibial shaft fractures without soft tissue injury. However, it has recently been replaced by IMN with locking screws. Plate osteosynthesis is still employed for proximal and distal tibia fractures when IMN is insufficient. Poor skin and soft tissue conditions, along with compromised blood flow, can complicate surgical decisions and lead to numerous complications. In elderly patients with osteoporosis and comminuted fractures, achieving stable fixation is challenging due to the reduced bone volume and quality. In such cases, a locking plate combined with pro-fibula screws may be used for tibial fixation [7,8].

Outcomes

Potential postoperative complications associated with plate osteosynthesis include non-union, delayed union, and wound infection. Studies comparing the outcomes of PLP and IMN are limited and inconsistent [8]. He et al. conducted a meta-analysis comparing minimally invasive percutaneous plates and interlocking

IMN for tibial shaft fractures. The study found that percutaneous plates led to faster healing and fewer postoperative complications, such as delayed union and pain. However, there were no significant differences in functional recovery, reoperation rates, or other complications between the two methods. Further high-quality, multicenter randomized controlled trials are needed to better compare these methods and optimize patient management [11].

Comparative studies

Table 2 provides a comparative summary of studies evaluating IMN, external fixation, and plating techniques for the treatment of tibial shaft fractures.

Table 2: Comparative analysis of fixation methods for tibial shaft fractures—IMN, external fixation, and plating

IMN vs external fixation					
Study	**Patients**	**Fracture Type**	**Result (IMN vs EF)**		**Conclusion**
Mohseni et al. (2011) [12]	n=50	Gustilo type IIIA & IIIB	Post-operative infection	16 vs. 32%; p=0.19	IMN is associated with fewer infections and healing problems, and faster recovery time compared to EF
			Soft tissue injury	8 vs. 12%; p=0.50	
			Malunion	0 vs. 24%; p=0.02	
			Nonunion	4 vs. 8%; p=0.50	
			Mean ambulation time after the operation	2.92 ± 2.43 vs. 2.68 +/- 2.14; p = 0.71	
Haonga, et al (2020) [13]	n=240	Diaphyseal open tibial	Death or reoperation	18.0 vs. 21.9%; RR=0.83 [95% CI, 0.49 to 1.41]; p = 0.505)	
			Rate of deep infection	No significant difference	IMN is associated with a lower risk of coronal malalignment and better early radiographic healing compared to EF. No significant difference in deep infection rates or overall primary outcome events.
			Coronal malalignment (Lower risk with IMN)	RR=0.11; p=0.01	
			Sagittal malalignment (Lower risk with IMN)	RR=0.17; p=0.065	
			Quality of life (EQ-5D)	Higher with IMN at 6 weeks, no difference at 1 year	
			Radiographic healing (mRUST)	Better with IMN at Better at 6 weeks, 12 weeks, and 1 year	
Kisitu et al. (2022) [14]	n=55	Gustilo-Anderson type II & IIIA	Functional outcome (FIX-IT score)	1.0-point higher for IMN	IMN provides marginal improvements in functional outcomes and significantly reduces malunion and superficial infection compared to EF
			Health-related quality of life (EQ-5D-3L & EQ-VAS)	Similar results for both groups	
			Radiographic healing (RUST)	No difference between both groups	
			Malunion rate	22.1% (95% CrI, –42.6% to 1.7%) lower for IMN	
			Superficial infection	20.8% (95% CrI, –44.0% to 2.9%) lower for IMN	
IMN vs plating					
			Results (IMN vs plating)		
Vallier et al. (2011) [15]	n=104	Extra-articular distal tibia shaft fractures	Deep infection	5.8% in both groups	Malalignment was more common with nails, especially in open fractures. Nonunion and infection rates were similar between the two methods.
			Nonunion	7.1% vs. 4.2%; p=0.25	
			Trend: Higher nonunion in patients with distal fibula fixation	12% vs. 4.1%, p = 0.09	
			Primary angular malalignment of ≥5°	23% vs. 8.3%; p= 0.02	
			Secondary procedures	14 procedures (IMN) vs. 15 procedures (Plating)	
Vallier et al. (2008) [16]	n=111	Extra-articular distal tibia fractures (4 to 11 cm proximal to the plafond)	Osteomyelitis	5.3% vs. 2.7%; p=0.10	Plating is associated with fewer cases of malalignment and delayed union compared to IMN. Similar rates of infection and hardware removal.
			Delayed union or nonunion	12 vs. 2.7%; p=0.10<	
			Angular malalignment ≥5 degrees	29 vs. 5.4%; p=0.003	
			Painful hardware removal	7.9 vs 5.4%	

Study	Patients	Fracture type	Result (IMN vs. EF)		Conclusion
Kang et al. (2021) [17]	n=73	Closed extra-articular tibial shaft fractures (AO/OTA type 42)	Bone Healing	1 case of nonunion in each group (p>0.05)	IMN and MIPO showed no significant differences in radiological and clinical outcomes, both being equally effective for treating tibial shaft fractures.
			Callus Formation	Mean 12 weeks in both groups (p>0.05)	
			Operative Time	No significant difference (p>0.05)	
			Hospital Stay	No significant difference (p>0.05)	
			Complications	No significant difference (p>0.05)	
			Functional Evaluation	No significant difference (p>0.05)	
Plating vs External fixation					
			Results (Plating vs EF)		
Krupp et al., 2009 [18]	n=58	Schatzker V/ VI or AO/OTA type 41C	Time to Union	5.9 months vs. 7.4 months	Locked plating showed faster union, fewer cases of articular malunion, less knee stiffness, and lower overall complication rates compared to external fixation. External fixation is used as a temporary measure until definitive fixation with plating can be performed.
			Articular Malunion	7% vs. 40%; p=0.003	
			Knee Stiffness:	4% vs. 13%	
			Overall Complications	27% vs. 48%	
			Schatzker VI Subgroup complications	93% vs. 83%	
Comparison of intramedullary nail, plate, and external fixation in the treatment of distal tibia nonunions					
Ebraheim et al., 2017 [19]	n=33	AO/OTA 43A & distal third 42A-C nonunions	Mean Time to Union (without revision fixation)	IMN: 12 weeks, PO: 27 weeks, EF: 13 weeks (p = 0.202)	Time to union was notably shorter when no revision fixation was required. IMN and PO were effective fixation methods, achieving significantly faster union times compared to EF. The time to union was further prolonged with a change in fixation method rather than an exchange of the same method, especially in cases with deep infections.
			Mean Time to Union (with revision fixation)	IMN: 17 weeks, PO: 21 weeks, EF: 66 weeks (p = 0.009)	
			Weeks to the union from nonunion diagnosis (all 29 healed nonunions)	IMN: 14 weeks, PO: 23 weeks, EF: 72 weeks (p = 0.009)	
			Revision Fail Rates	IMN: 0%, PO: 25%, EF: 71%	
			Time to Union (revision method change vs. the same method)	51 weeks vs 18 weeks (p = 0.030)	

IMN: Intramedullary Nailing; EF: External Fixation; PO: Plate Osteosynthesis; VLP: Volar Locking Plate; MIPO: Minimally Invasive Plate Osteosynthesis; mRUST: Modified Radiographic Union Score for Tibia; RUST: Radiographic Union Score for Tibia; EQ-5D: EuroQoL Five-Dimensional Scale; EQ-VAS: EuroQoL Visual Analog Scale; FIX-IT: Functional Index for Extremity Injuries; DASH: Disabilities of the Arm, Shoulder, and Hand; VAS: Visual Analog Scale; AO/OTA: Arbeitsgemeinschaft für Osteosynthesefragen / Orthopaedic Trauma Association
CrI: Credible Interval; CI: Confidence Interval.

Conclusion

The management of tibial shaft fractures, especially open fractures, requires careful assessment of various fixation strategies: IMN, external fixation, and plating. Each method has unique advantages and considerations based on fracture severity and soft tissue involvement. IMN is often preferred for its biomechanical stability and minimal soft tissue disruption. It allows for early fracture stabilization and is particularly effective for diaphyseal fractures and select open fractures where timely wound closure is possible. External fixation provides rapid stabilization, which is essential for severe soft tissue injuries or when immediate definitive fixation is not feasible. However, it is associated with a higher risk of complications, including pin tract infections and malunion. Plating, although rarely used for tibial shaft fractures, is useful in cases that require additional fixation strength, especially for specific fracture patterns or when IMN is unsuitable due to soft tissue concerns. The choice of fixation method ultimately depends on individual patient factors, fracture characteristics, and the surgeon's expertise. The goal is to minimize complications such as nonunion, malunion, and infection. Further studies and advancements in techniques will continue to improve treatment approaches for these complex injuries.

Article information

Conflicts of interest

The authors have no conflict of interest to declare.

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Data availability

Data of this study are available from the author/s upon reasonable request.

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Review article

ARIF an Alternative to ORIF in the Management of Tibial Plateau Fractures: A Narrative Review

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Abstract

Tibial plateau fractures, caused by valgus or varus impact with axial compression or torque force, result in complex injuries of the intra-articular and metaphyseal aspect of tibia. These fractures can lead to intra-articular chondral damage, meniscal tear, ligament rupture etc. Treatment choice depends on fragment displacement, subchondral bone involvement, injury severity, associated injuries, and patient characteristics. Successful treatment mandates anatomical reduction, stable fixation, minimal invasiveness, and restoration of postoperative range of motion. Inadequate treatment may lead to pain, joint instability, restricted motion, and substantial disability. Comprehensive understanding of the fracture is crucial for effective management. Surgical strategies aim to achieve for meticulous fracture reduction while minimizing morbidity and avoiding additional damage. Traditionally, open reduction and internal fixation (ORIF) using plates and screws has been a standard treatment. However, ORIF is associated with complications such as infections, stiffness, pain etc. Arthroscopically assisted reduction with percutaneous internal fixation (ARIF) has emerged as a promising alternative, offering lower morbidity, precise reduction assessment, improved intra-articular lesion treatment, shorter hospital stays, lower infection rates, and better functional scores compared to ORIF.

Keywords: Tibial plateau; fractures; Surgical treatment; ORIF; ARIF; arthroscopy

Tibial plateau fractures: An overview

Tibial plateau fractures are complex injuries involving the intra-articular and the metaphyseal segments proximal tibia. They typically result from either a valgus or varus force, along with axial compression. These forces are frequently accompanied by torque, adding to the complexity of the injury, or can occur due to forces of multiple direction [1–3]. In most cases, either the medial or lateral femoral condyle acts as an anvil, applying a combination of both shearing and compressive force to the underlying tibial plateau [3]. In young adults, tibial plateau fractures are often a result of high-energy trauma, whereas in the elderly population, particularly those with osteoporosis, these fractures may occur due to low-energy injuries [4]. Splitting and depression fractures are more common in patients after the fifth decade. Tibial plateau fractures often affect proximal tibial metaphysis and articular surface [5]. Due to the injury mechanism, these fractures are often associated with intra-articular lesions such as chondral damage, meniscal tear, and ligament rupture [6].

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Prevalence of tibial plateau fractures

Incidence of tibial plateau fractures associated with proximal tibial metaphysis comprise 1.2% of all the tibial plateau fractures [5]. The prevalence of tibial plateau in adults is approximately 1%–2%, compared to 8% in the elderly population fractures [5,7].

Classification of tibial plateau fractures

While tibial plateau fractures make up only 1% of all fractures, they encompass a wide range of injuries that could have severe consequences if not treated appropriately [2]. Inadequate treatment may result in pain, joint instability, restricted range of motion, and severe disability with a significant negative social impact [2,6]. The successful treatment of tibial plateau fractures relies on a comprehensive understanding of the fracture pattern [2]. Orthopedic surgeons commonly utilize the Schatzker classification system for tibial plateau fractures in clinical practice (Table 1) [2].

Management of tibial plateau fractures

The goal of tibial plateau fracture treatment

While each fracture is different from the others, the main goals of the treatment remain the same: anatomical reduction, stable fixation, loose body removal, minimal invasiveness, repair of soft tissue injuries, postoperative unrestricted range of motion, etc [2,10]. The crucial element in treating these fractures is not only restoring the mechanical axis of the lower limb and achieving an anatomically reduced articular surface but also minimizing complications and having the ability to attain functional capability [4]. The surgical strategy should aim for a meticulous reduction of the fracture, minimizing morbidity, and avoiding additional damage, particularly to the local blood supply. Simultaneously, the approach must facilitate optimal visualization for the repair. The implants should be able to provide a stable construct allowing proper tissue closure and healing [5].

Surgical approach in the management of tibial plateau fracture

Management of tibial plateau fracture is challenging due to the complex fracture pattern and associated complications. The choice of surgical treatment depends on the displacement of the bony fragments, the pattern of involvement of subchondral bone, the severity of the lesion, associated soft-tissue damage, knee instability, meniscal lesions, the possibility of compartment syndrome, bone quality, patient's age, lifestyle, etc [1].

Different surgical approaches have been developed and used for the treatment of tibial plateau fractures, these include minimally invasive plate osteosynthesis (MIPO), closed reduction and internal fixation (CRIF) open reduction and internal fixation (ORIF), fluoroscopy-assisted procedures, and arthroscopic and arthroscopically assisted reduction, internal fixation (ARIF) anterolateral approach and posteromedial inverted L-shape approach [2,4,7,10,11].

ORIF in the management of tibial plateau fracture

ORIF with plates and screws, have been used for decades for the management of tibial plateau fractures [12]. However, complications such as infections, hematoma formation, surgical wound dehiscence, knee stiffness, neurovascular injury, thrombosis, soft tissue injuries, severe postoperative pain, and the presence of scar-related complications are common with ORIF [4,11,13]. The outcomes of the treatment are impaired by the restriction of articular motion, lack of articular congruence, stability, or alignment restoration [5]. A retrospective study collected 214 cases of tibial plateau fractures and found that infection occurred in 12% of patients after ORIF. Of the 12%, 9% of the patients suffered from deep infections [13].

ARIF in the management of tibial plateau fracture

The last decades' literature has shown the effectiveness of arthroscopically assisted treatment [12]. ARIF is the minimally invasive technique that has recently been recognized as an alternative to ORIF, with a lower morbidity rate, precise reduction assessment, and treatment of additional intraarticular lesions for patients with Schatzker type I–III fractures [2]. It provides direct visualization of the joint space, allowing for improved control of articular surface reduction and the opportunity to assess and address associated intra-articular lesions [6]. In comparison to open treatment, arthroscopy does not require meniscal detachment and repair. It allows for the evacuation of hemarthrosis and fracture debris. Furthermore, it leads to rapid recovery, reduction in pain, early regain of full range of motion, improved fracture healing, and more complete and functional recovery [3]. Moreover, ARIF enables surgeons to address both plateau fractures and intra-articular soft tissue concurrently [13]. Complications of ARIF like compartment syndrome, fluid extravasation, etc cannot be overlooked, though it can be minimized with progress in learning curve.

Clinical overview of ARIF and ORIF for the management of tibial plateau fracture

The studies including Schatzker I–III fractures found equal or superior results of ARIF compared to ORIF with a lower rate of complications, shorter hospital stay, lower infection rate, better knee society score, and Rasmussen's radiological score [9]. A systemic review compared complication rates in ORIF vs. ARIF group for plateau fractures. The study reported that the complication rates were higher in the ORIF group compared to the ARIF group (9.1% vs 5.6%) [13]. Research findings have indicated favorable functional and radiological outcomes in the short to medium term following ARIF [8]. The detailed outcomes of the studies are mentioned in Table 2.

Conclusion

ARIF in comparison to ORIF in the management tibial plateau fractures has consistently shown favorable

Table 2: Clinical overview of ARIF vs. ORIF

Study Method			**Result (ARIF vs. ORIF)**		**Conclusion**	**Reference**
Number of patients (ARIF vs. ORIF)	**Schatzker type**	**Follow-up (months)**				
50 vs. 50	I–VI	12 to 116	Rasmussen clinical score	27.62 vs. 26.81	ARIF and ORIF techniques have similar outcomes. However, ARIF is preferred due to the lower rate of infection.	[1]
			Rasmussen radiological score	16.56 vs. 15.88		
			Hospital for Special Surgery score	76.36 vs. 73.12		
			Superficial infection (n)	0 vs. 2		
			Deep infections(n)	0 vs. 2		
40 vs. 35	I–III	13.5	Duration of hospital stay	3.10 vs. 5.51 days ($p = 0.0001$)	ARIF and ORIF resulted in similar outcomes however treatment with ARIF reduced the duration of hospital stay.	[2]
			No statistically significant difference in average clinical and radiological Rasmussen scores between the two groups.			
33 vs. 35	II or III	36	Duration of hospital stay	3.58 vs. 4.57 days ($p = 0.002$)	ARIF was found to be safe, effective, reliable, and safe. ARIF resulted in more precise evaluation and reduced the duration of hospital stay compared to ORIF.	[8]
			International Knee Documentation Committee score, Hospital for Special Surgery score, Range of motion were similar in both the groups			
231 vs. 386			Better clinical function	SMD = 0.31; 95% CI, 0.14 to 0.48; $I^2 = 15\%$; $p = 0.0005$	ARIF when compared to ORIF led to faster postoperative recovery, better clinical function, and could find and treat more intra-articular lesions.	[11]
			Shorter hospital stay	MD = −2.37; 95% CI, −2.92 to −1.81; $I^2 = 0\%$; $p < 0.001$		
			More intra-articular lesions found intraoperatively	OR = 3.76; 95% CI, 1.49 to 9.49; $I^2 = 66\%$; $p = 0.005$		
			Radiological evaluation of reduction and complications were similar in both groups.			
19 vs. 21	I–III	44.4	Mean duration of hospital stay	3.95 vs. 5.86 days ($p < 0.05$)	ARIF led to better clinical results than ORIF.	[12]
			Mean Knee Society Score	92.37 vs. 86.29 ($p<0.05$).		
			Rasmussen radiographic score	8.42 vs. 7.33 ($p = 0.104$)		
			No statistically significant differences were found in perioperative complications, radiological results, and post-traumatic knee osteoarthritis.			

Study Method			**Result (ARIF vs. ORIF)**		**Conclusion**	**Reference**
Number of patients (ARIF vs. ORIF)	**Schatzker type**	**Follow-up (months)**				
321 patients, treated with ARIF		74.8	The mean posterior slope angle increased from 9.3° to 9.6° (p=0.092).		Most patients achieve excellent and good clinical outcomes and low complication rates with ARIF.	[13]
			4.3% of patients experienced superficial or deep infection			
			Total knee arthroplasty was performed in 2.2%			
			97.8% of patients had good or excellent results in the Rasmussen radiologic assessment			
			96.7% of patients had good or excellent results in the Rasmussen clinical assessment			
57	I–IV	44.4	Rasmussen radiographic score	14.1 vs. 14.9 (p < 0.05)	ARIF and ORIF yielded satisfactory clinical results. ARIF led to better radiological results than ORIF.	[14]
			Superficial infection (n)	0 vs. 1		
			Knee Society Score	No significant difference		
			Rasmussen clinical score			
1272	I–III	≥ 24	Better post-operative functional outcomes	SMD=1.23, 95% CI, 1.08–1.38; p<0.00001	ARIF was associated with better functional outcomes, a lower risk of perioperative complications, and a lower risk of post-traumatic osteoarthritis.	[15]
			Lower post-traumatic osteoarthritis	OR=0.24, 95% CI, 0.08–0.72; p=0.01		
			Perioperative complications (n)	12 vs. 36		

ARIF - Arthroscopy assisted reduction percutaneous internal fixation; ORIF - Open reduction internal fixation; SMD - Standardized mean difference; MD - Mean difference; OR – Odds ratio.

outcomes. ARIF demonstrates similar or superior results in terms of clinical function, Knee Society Score, and radiological scores. The length of hospital stay and infection rates were lower in the ARIF group compared to ORIF. Notably, ARIF was associated with faster recovery, reduced pain, and improved overall functional recovery compared to ORIF. Meta-analysis results further support the superiority of ARIF in terms of postoperative functional outcomes, lower perioperative complications, and reduced risk of post-traumatic osteoarthritis. ARIF was considered a safe, effective, and minimally invasive alternative to ORIF for managing tibial plateau fractures that offered advantages of precise reduction assessment, treatment of intra-articular lesions, and improved patient outcomes.

Article information

Conflicts of interest

The authors have no conflict of interest to declare .

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Data availability

Data of this study are available from the author/s upon reasonable request.

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