



Emerging Technologies in Distal Radius Fracture Fixation

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Abstract

Purpose of Review To provide an overview of emerging fixation constructs and materials used in the operative management of distal radius fractures.

Recent Findings The indications, advantages, and disadvantages of relatively new implants and devices used to treat distal radius fractures are discussed. These include the intramedullary nail, intramedullary cage, radiolucent volar locking plate, distal radius hemiarthroplasty, and bone graft substitutes.

Summary The spectrum of distal radius fracture patterns may make it impossible to depend on a single device for fixation, and surgeons managing distal radius fractures should be adept at using various surgical approaches, techniques, and hardware systems. Additional studies demonstrating the cost-effectiveness, biomechanical properties, and clinical outcomes will be useful in determining the utility of the described techniques.

Keywords Distal radius fracture · Internal fixation · Bone graft

Introduction

Distal radius fractures are vastly heterogeneous in their mechanisms of injury and fragmentation patterns. The technical goals of surgical treatment include the restoration of length, alignment, and inclination, as well as reduction of articular incongruity at the radiocarpal and the distal radioulnar joints. In appropriately selected patients, operative treatment offers superior outcomes compared with non-operative care in terms of anatomic reduction and grip strength [1] and can avoid complications of closed treatment such as malunion and weakness [2].

Although numerous fixation constructs are currently used, volar locking distal radius plates are the most popular [3, 4]. The introduction of volar locking plates has led to excellent patient-rated and objective outcomes [1, 5, 6]; however, a new set of complications have surfaced. These complications include flexor and extensor tendon rupture [7, 8], loss of fixation [9], intra-articular screw placement [10], flexor tendon adhesions [11], and wrist flexion contracture requiring hardware removal and surgical release [12].

Furthermore, not all distal radius fractures are amenable to volar plate fixation. For example, isolated radial styloid fractures, volar lunate facet fractures, dorsal shear fractures, dorsal ulnar facet corner, and severely comminuted intra-articular fractures are typically treated with devices other than a volar locking plate [13]. Other commonly used fixation methods include bridging and non-bridging external fixation [14–16], Medoff's fragment-specific fixation [13], and bridge plates in the setting of severely comminuted distal radius fractures or polytrauma patients [17].

The desire to improve fixation and minimize iatrogenic injury, as well as the appeal of early return to function have, in part, driven the development of new technologies in distal radius fracture fixation [18]. This review will discuss emerging fixation constructs and materials in the operative management of distal radius fractures.

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Intramedullary Nails

Gerhard Kuntscher is credited with the development and popularization of modern intramedullary nailing (IMN) techniques of the lower extremity [19]. Rigid intramedullary fixation is desirable as it spares the extraosseous blood supply, minimizes soft tissue dissection, reduces time of immobilization, and allows earlier weight bearing owing to its load-sharing biomechanical properties [20]. Lower extremity intramedullary nailing of diaphyseal fractures has a proven track record due to decades of experience and implant refinement. Rigid intramedullary nailing of the distal radius, however, is a relatively recent advent, making its appearance in the literature in 2005 [21].

There are currently a number of intramedullary nails on the market globally, like the Micronail II (Wright Medical, Arlington, TN) (Fig. 1), the Targon DR Nail (B. Braun, Melsungen, Germany), and the Sonoma Wrx (Sonoma Orthopedic Products, Santa Rosa, CA). The concepts behind their development, indications, and technique are similar. Intramedullary nailing of the distal radius is indicated for extra-articular and simple intra-articular fractures. Attempting to nail



Fig. 1 Micronail (Wright Medical, Arlington, TN), 3 years postoperatively (courtesy of Adam B. Strohl, MD, Philadelphia Hand to Shoulder Center)

small extra-articular fragments [11] and multi-fragmented intra-articular distal radius fractures may be problematic as it is difficult to capture smaller fragments [22•]. The nail is generally fabricated from titanium alloy, has fixed angle distal locking screws for subchondral support, and features diaphyseal interlocking bicortical screws to control length and rotation [21].

Capo et al. conducted a biomechanical study and compared volar locking plating with IMN in an extra-articular, dorsally comminuted fracture model [23]. The testing was performed on 28 cadaveric specimens and demonstrated that a volar locking distal radius plate (DVR plate, Hand Innovations) exhibited higher bending stiffness (16.7 N/mm vs. 12.6 N/mm) and load to failure (278.2 N vs. 245.7 N) and withstood more load to cause 5 mm of displacement (95.2 N vs. 75.6 N) than a Micronail IMN. None of these differences were statistically significant, however.

In another biomechanical study of an extra-articular fracture model, Burkhart et al. compared the Targon with a 2.4-mm titanium locking compression plate (LCP) (Synthes, Freiburg, Germany), which is not commonly used to treat distal radius fractures [24]. Axial loading revealed that intramedullary osteosynthesis was significantly stiffer than plate osteosynthesis (369 N/mm vs. 131 N/mm, respectively; $p = 0.017$). The intramedullary nail also showed higher stability with dorsal eccentric loading relative to the locking compression plate (214 N/mm vs. 51 N/mm, respectively; $p = 0.012$). The load to failure tests demonstrated significantly higher stability of intramedullary nailing (625 N) when compared with plate osteosynthesis (403 N). However, based on a review of the literature, Jordan et al. noted that there was insufficient high-quality data to demonstrate the superiority of IMNs over volar locking plates [25].

The surgical technique requires the fracture to be reduced by closed means. Next, preliminary stabilization with Kirschner wires is performed. A 2–4-cm incision is made over the radial styloid, and branches of the dorsal radial sensory nerve (DRSN) are dissected and protected. The plane between the first and second dorsal compartments is developed. The cortex at the radial styloid is then opened, and broaches are used sequentially. An appropriately sized nail is then inserted in a retrograde fashion, and reduction is confirmed. Next, the proximal and distal locking screws are placed using the appropriate targeting guides.

The potential complications of distal radius IMN include DRSN irritation [22•, 26, 27], errant screw placement into the distal radioulnar [22•, 26, 28] and radiocarpal joints, possible loss of reduction of small extra-articular fragments resulting in increased dorsal angulation, decreased radial inclination or shortening, and loss of articular fragment reduction [11, 22•, 27, 28].

Ilyas and Thoder reported a series of 10 cases with follow-up of 21 months [26]. Wrist range of motion and grip strength were encouraging, and a DASH score of 8.1 was obtained. Volar tilt was -2.2° , while the average variance measured -0.6 mm.

Loss of reduction occurred in 2 patients, 2 cases developed transient DRSN irritation which resolved by 12 weeks, and 3 cases of screw penetration into the distal radioulnar joint (DRUJ) occurred, causing symptomatic arthritis in one patient.

Gradl et al. performed a randomized trial of 14 volar plates versus 14 Targon IMN for simple intra-articular distal radius fractures with metaphyseal comminution [22•]. No differences in the range of motion (ROM) at 8 weeks as well as ROM and grip strength at 2 years were noted. While ulnar variance (-0.4 mm vs 0.8 mm) and volar tilt (5.5° vs 0.0°) were significantly better at 2 years in the volar plate group, no differences in functional or pain outcomes were identified. Complications in the IMN group included screw penetration into the DRUJ and transient DRSN neurapraxia. The authors suggested that IMN may provide better maintenance of fracture reduction in extra-articular and simple intra-articular fractures [22•].

In a different study, Gradl et al. looked at displaced extra-articular fractures and randomized treatment to either IMN (Targon) or 2.4 mm volar plate fixation [27]. Similar outcomes at 2 years were noted for grip strength, ROM, pain scores, Gartland and Werley scores, Castaing score (wrist function and radiographic data), ulnar variance, and volar tilt. There was one case of screw penetration into the DRUJ when the IMN was used. DRSN neurapraxia occurred in 8 IMN cases and 7 volar plate cases, secondary to Kirschner (K) wire placement through the styloid.

In a level II prospective randomized study, Plate et al. compared the Micronail with a 2.4-mm volar plate [11]. No differences in short-term results for up to 2 years were noted when comparing the Michigan Hand Questionnaire (MHQ), Quick Disabilities of the Arm, Shoulder and Hand (QDASH), grip strength, and pinch strength. Furthermore, no differences in narcotic pain medication use in the first month were noted. Patients who underwent IMN had improved wrist extension at 6 weeks (70° vs 51°), but no other differences were found. Of interest, the authors reported one case of intraoperative conversion from IMN to open reduction and volar plate fixation in order to obtain adequate fracture reduction. The authors also cautioned that small extra-articular fragments may not be adequately stabilized with an IMN construct.

Intramedullary Cage Constructs

The Cage Distal Radius System (Conventus Orthopedics, Maple Grove, MN) features an expandable implant that is deployed into the medullary canal of the distal radius (Fig. 2). It provides a scaffold to which bone fragments can be stabilized using fragment-specific screws [18•]. The implant is fabricated from nitinol (nickel-titanium alloy). The temperature-dependent characteristics of nitinol allow the intramedullary cage to be delivered in a compressed state and then fully recover its expanded set shape and full material strength within the medullary space at body temperature [29].

This device is indicated primarily for extra-articular and simple intra-articular distal radius fractures. In theory, the advantages of the cage system include fixed angle fixation, subchondral support, load-sharing properties, intramedullary placement of the fixation construct, limited incisions, and minimization of soft tissue stripping. The potential disadvantages include soft tissue irritation from prominent screws. In addition, hardware removal may be necessary for a variety of reasons, including infection, symptomatic implants, or the need for future salvage with wrist arthroplasty or arthrodesis. The shape and fixation mode of this implant raises concerns related to subsequent hardware removal in the setting of bone ongrowth and ingrowth. It is the opinion of the authors that more studies are required to demonstrate the nature of hardware removal and the capacity to preserve bone stock when removing this implant.

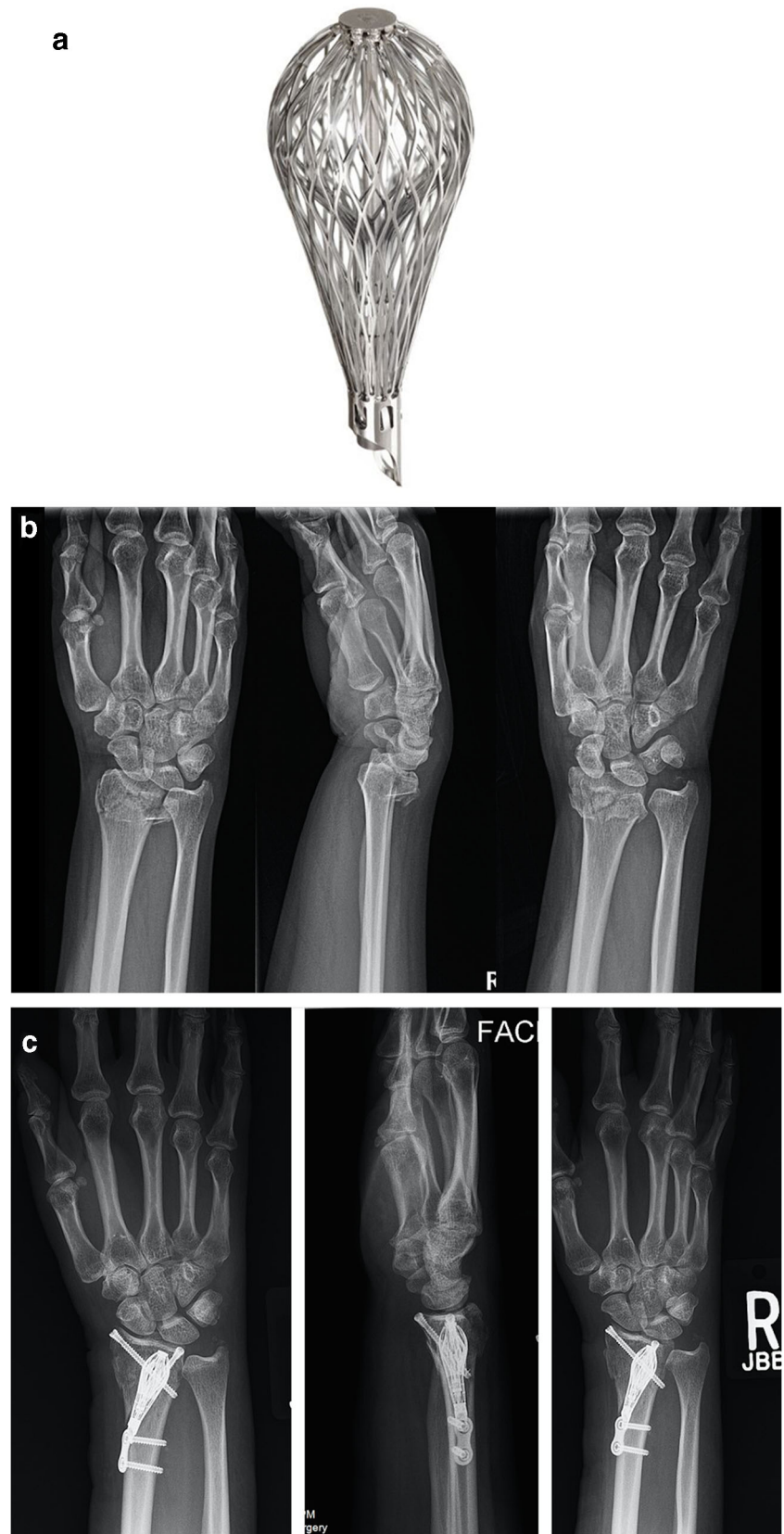
van Kampen et al. performed a biomechanical study comparing the stiffness and stability of a titanium volar locking plate (Depuy Orthopedics, Warsaw, IN) and the Cage Distal Radius System (DRS) implant [29]. A dorsally comminuted, extra-articular, distal radius sawbones fracture model was used. Under axial loading to 250 N, eccentric loading, and cyclic loading, no differences in stiffness or failure were detected between the intramedullary cage and the volar locking plate construct.

In the clinical setting, Strassmair et al. reported their outcomes in a case series of patients treated with the intramedullary cage [18•]. A total of 100 patients with extra-articular and simple intra-articular fractures—including those with metaphyseal comminution—were assessed. The patients were followed for 12 months. The DASH scores at 3 and 12 months were 21 and 9, respectively. Similarly, wrist ROM gradually improved up to 12 months, with near normalization relative to the contralateral, unaffected side. There was a 5% complication rate including DRSN irritation and tendon irritation. There were no cases of nonunion or infection. At 12 months of follow-up, ulnar variance measured $+0.5$ mm, volar tilt -1.4° , and radial inclination 19.7° . Hardware removal was possible up to 444 days postoperatively, reportedly without causing additional damage to surrounding tissues [18•].

PEEK Volar Locking Plates

The earliest publications of the use of polyether etherketone (PEEK) in orthopedic implants were reported in the 1980s [30, 31]. Carbon fiber-reinforced polyether etherketone (CFR-PEEK) materials are considered to be relatively inert in a biological context and have undergone extensive biocompatibility testing [32]. PEEK implants have been used in orthopedic fracture plates and intramedullary nails, bone anchors, and plates for partial wrist fusions [33–35]. Distal radius volar locking PEEK systems typically consist of a PEEK plate and titanium screws that thread into the plate to create a fixed angle fixation construct [33].

Fig. 2 **a** Conventus DRS implant (Conventus Orthopedics, Maple Grove, MN). **b** Pre-operative radiographs of a comminuted, intra-articular and dorsally angulated distal radius fracture (courtesy of ©Scott W. Wolfe, MD, 2019). **c** Postoperative radiographs of the patient in **(b)** demonstrating fracture fixation with the Conventus DRS implant (courtesy of ©Scott W. Wolfe, MD, 2019)



PEEK volar plating provides radiolucent fixation as its primary advantage, which in theory may be helpful for intraoperative evaluation of fracture reduction and postoperative assessment of callous formation [36•] (Fig. 3). In addition, the plastic plate has a low interference footprint with magnetic resonance imaging and computed tomography [37], limiting hardware artifact and enabling enhanced assessment with these imaging studies. PEEK has a modulus of elasticity similar to cortical bone, thereby minimizing stress shielding. This has implications for hardware removal, as stress-shielded bone tends to have a lower bone mineral density and may be more susceptible to refracture in the first few months following hardware removal [38]. These plate constructs offer sufficient rigidity to promote bone healing, yet excessive flexibility may be problematic, potentially leading to pseudarthrosis [33, 34].

The use of plastic and metal eliminates the risk of cold welding between screws and plate, which may become problematic in titanium constructs that have remained in the bone for a few years [39]. Similar to traditional metallic volar plates, polyaxial screws capable of stabilizing various fragments offer yet another advantage. Concerns about wear debris from the PEEK plate causing local inflammatory reactions persist, although a laboratory study by Steinberg et al. demonstrated a lower wear debris weight for a PEEK-OPTIMA plate relative to a titanium control [40]. Additional disadvantages similar to conventional metallic volar plates exist. These include concerns about tendon rupture, intra-articular screw placement, and loss of fixation [33].

The locking screw feature limits the number of attempts at redirecting the screw through the plate and this may become a limitation in theory. Biomechanical studies on sawbones models have demonstrated the CFR-PEEK DiPHOS-RM distal radius plate (Lima Corporate, San Daniele Del Friuli, Udine, Italy) to be more brittle than titanium alloy or stainless steel plates, as evidenced by little tolerance to plastic deformation [33]. This is consistent with the fact that PEEK plates cannot be contoured [34]. While plate radiolucency may be advantageous for assessing fracture reduction and callous formation, radiolucency compromises visualization of plate positioning and plate failure. To circumvent these problems, some plates have incorporated radio-opaque markers [41•].

DiMaggio et al. performed a multicenter study assessing the 12-month outcomes of 64 patients treated with the Piccolo CFR-PEEK radiolucent volar plate (Unimedical Biomedical Technologies, Torino, Italy). The mean age at surgery was 56.8 years, and the fractures were all classified as either AO type B or C (simple and complex intra-articular fractures, respectively). The Modified Mayo Wrist Score improved from 38.1 at 1 month to 67.2 at 2 months, and to 90.5 at 12 months following surgery. There were no cases of malunion, nonunion, infections, or flexor tendon injury. There was one case of screw loosening that necessitated hardware removal at 5 months postoperatively [41•].

In a randomized trial, Perugia et al. compared the outcomes of 15 patients treated with a Carbofix volar locking plate (Carbofix Orthopedics, Herzeliya, Israel) to the outcomes of patients treated with a titanium volar plate (Acumed, Hillsboro, OR). The mean follow-up was 15.7 months for the PEEK group and 16.1 months for the titanium group. No statistically significant differences were noted for grip strength, wrist flexion, wrist extension, forearm rotation, DASH, pain scores, and radiographic parameters. No postoperative complications were noted in either group [36•].

While the laboratory and clinical studies on PEEK volar plates appear to be encouraging, clinical outcomes remain in their short-term, and longer follow-up will be required. Furthermore, consistently favorable outcomes, as well as studies that objectively demonstrate the benefits of PEEK plates over metallic plates, will be useful in promoting the utility of these implants.

Distal Radius Hemiarthroplasty

Upper extremity joint replacement for severely comminuted, intra-articular osteoporotic fractures is known to be effective in the treatment of appropriately selected patients with proximal humerus fractures (hemiarthroplasty or reverse total shoulder) and distal humerus fractures (total elbow arthroplasty). This concept has been extrapolated to treat distal radius fractures and appears to have been first published by Roux in 2009 [42]. The treatment concept is based on the replacement of the comminuted radiocarpal, and at times the distal radioulnar articular surfaces, restoring radial length and offering immediate stability [42, 43, 44•, 45, 46•] (Fig. 4).

The indications include primary treatment of comminuted, osteoporotic, intra-articular fractures, as well as treatment following failure of distal radius open reduction and fixation [44•]. In brief, the surgical technique requires a wrist dorsal approach, typically between the third and fourth dorsal compartments, exposure of the fracture and the radius more proximally, excision of the epiphyseal fracture fragments, and metaphyseal distal radius resection. Broaching and trialing are then performed. Once the appropriate-sized trial has been determined, the implant may be cemented [46•] or press-fitted into place [44•].

Herzberg et al. reported their distal radius hemiarthroplasty results on 12 wrists in 11 patients, treated for acute AO type C intra-articular fractures [44•]. All patients were over 65 years old and lived independently at the time of surgery. The Remotion (Stryker, Kalamazoo, MI) radial component and the Cobra system (Groupe Lépine, Lyon, France) were used. If sigmoid notch repair with suture fixation was not possible, the ulna head was excised. Press-fit fixation of the implant was obtained in this series, and the patients were immobilized for 3 weeks postoperatively. The mean follow-up duration for these 12 cases was 32 months (range, 24–44 months). In addition, a second group of 4 patients underwent wrist hemiarthroplasty secondary to malunion or failure of previous

Fig. 3 **a** Pre-operative radiographs of a comminuted, dorsally angulated distal radius fracture. **b** Postoperative radiographs demonstrating fracture fixation with the NeoView PEEK distal radius plate (In2Bones, Memphis, TN). The radiolucent volar plate is transfixed by titanium cortical and locking screws. The proximal extent of the plate is indicated by a longitudinally oriented tantalum marker. **c** Intraoperative photograph of the NeoView PEEK distal radius plate



fixation, with of 3 months mean period between initial and secondary treatment. In the acute fracture group, 3 cases

developed transient complex regional pain syndrome, and re-operation for radial deviation deformity was performed in 1

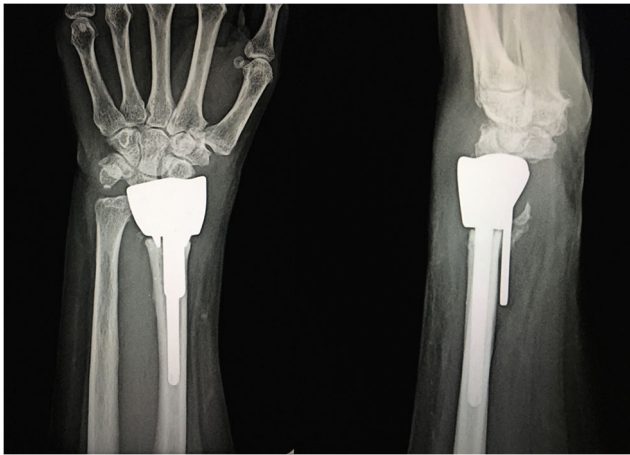


Fig. 4 Distal radius fracture hemiarthroplasty (Zimmer Biomet, Warsaw, IN) used to salvage failed open fixation of a comminuted intra-articular distal radius fracture (courtesy of Randall W. Culp, MD, Philadelphia Hand to Shoulder Center)

patient. The mean QDASH was 25, mean PRWE 22, mean pain score 1/10, and wrist flexion and extension were 62° and 35°, respectively. The mean pronosupination arc of motion was 149°. Grip strength measured 14 kg (69% of contralateral side). Consolidation was achieved in all implants, and no early loosening was detected. Similar but slightly inferior outcomes were observed for the 4 cases treated secondarily [44•].

Vergnenègre et al. retrospectively reviewed the outcomes of 8 patients with an average age of 80 years (74–85 years) [46•]. The mean follow-up duration was 25 months (17–36 months), and the fractures were all AO type C2 fractures. In this series, patients

with a distal ulna fracture were excluded because the cutting guide relied on an intact ulnar head. The Sophia distal radius implant (Biotech, Paris, France) was cemented into place, and the mean operative time was 66 min. Patients were immobilized in a short arm cast for 3 weeks, and then formal physical therapy was started at 6 weeks. In this series, patients were able to return to activities of daily living (ADLs) on average in 3 weeks (range, 0.5–5 weeks). The mean wrist flexion, wrist extension, and forearm rotation measured 45°, 44°, and 160°, respectively. Grip strength was 18 kg (90% of contralateral side), while the QDASH was 18.2. No cases of implant loosening or ulnar translocation of the carpus were noted [46•]. The authors suggested that hemiarthroplasty is a technically simpler procedure relative to open fixation of a comminuted, intra-articular distal radius fracture. Other potential advantages include earlier motion and return to ADLs, typically within 3 weeks [46•].

The outcomes of this novel procedure remain in their infancy, however, with the data being very limited. The disadvantages and complications associated with hemiarthroplasty for distal radius fractures have not yet been fully elucidated. It is reasonable to raise concerns about articular wear of the proximal carpal row secondary to metal-on-cartilage contact, carpal instability, bone loss in the setting of implant removal, and implant loosening.

Bone Graft Substitutes

The role of bone grafting in acute distal radius fracture fixation remains controversial as the scientific data in its support is very limited [47]. Some surgeons use bone graft to augment fixation

Table 1 Implant indications, advantages, and disadvantages

Device	Primary indications	Theoretical advantages	Theoretical disadvantages
Intramedullary nail	Extra-articular and simple intra-articular fractures	<ul style="list-style-type: none"> • Smaller incisions • Reduces risk of tendon injury and screw penetration into the joint • Minimizes soft tissue stripping, while permitting early motion 	<ul style="list-style-type: none"> • Less distal fixation • Increased risk for loss of reduction
Intramedullary cage	Extra-articular and simple intra-articular fractures	<ul style="list-style-type: none"> • Smaller incisions • Fixed angle fixation with subchondral support and load sharing • Intramedullary placement of fixation construct • Minimizes soft tissue stripping 	<ul style="list-style-type: none"> • Soft tissue irritation from prominent screws • Concerns related to bone loss during hardware removal in the setting of bone ongrowth
Radiolucent PEEK volar locking plate	Extra-articular, simple and complex intra-articular fractures	<ul style="list-style-type: none"> • Modulus of elasticity similar to bone • Improved visualization of fracture reduction and bone healing • No risk of cold welding between screws and plate • Low artifact interference with MRI and CT imaging 	<ul style="list-style-type: none"> • Cannot be contoured • Locking screws create threads into the plate, limiting the number of attempts at redirecting the screw • Concerns about excessive plate flexibility and plastic wear from screws • Similar soft tissue and fixation-related problems to metallic volar locking plates.
Distal radius hemiarthroplasty	Comminuted intra-articular fractures in elderly patients with osteoporotic bone, possible distal ulna fractures	<ul style="list-style-type: none"> • Early motion and weight bearing 	<ul style="list-style-type: none"> • Articular wear of the proximal carpal row • Carpal instability • Implant loosening • Increased bone loss if future salvage is required

in osteoporotic bone or buttress-impacted osteoarticular fragments that have lost metaphyseal support in addition to the use of volar plating or other types of fixation. When a volar locking plate is used, attempts are made to place the distal locking screws as close as possible to the subchondral bone to prevent subsidence of the distal radius [5, 48, 49]. Orbay and Fernandez suggested screw placement 3 mm or less from the articular surface [5]. Care should be taken to avoid joint penetration and intra-articular screw placement. Despite the use of fixed angle support in volar locking plates, complications such as loss of reduction, radial collapse, and radial shortening may occur, particularly with more complex intra-articular fracture types [50].

Numerous bone graft materials have been developed and may be applied to fill distal radius bone defects. While autograft is a desirable bone graft material given its osteogenic, osteoinductive, and osteoconductive properties, it is associated with donor site morbidities such as hematoma formation, infection, and even meralgia paraesthetica when taken from the iliac crest. In addition, harvesting autologous bone graft increases operative time [51]. When off-the-shelf products are used, some surgeons prefer to use cancellous chips or putty, while others prefer to use injectable bioactive cement that subsequently hardens. When the latter is used, care should be taken to avoid cement extrusion into the radiocarpal joint or adjacent soft tissues.

Kim et al. compared the outcomes of 21 patients over 65 years of age treated with volar plating and calcium phosphate bone cement (CPC) augmentation and 20 patients with plate fixation only [52]. The patients that underwent CPC injection demonstrated radiographic incorporation of the cement into host bone. At 12 months of follow-up, however, no differences in functional DASH outcomes, pain scores, ROM, grip strength, or radiographic outcomes such as radial inclination, ulnar variance, or volar tilt were detected.

Hegde et al. used hydroxyapatite augmentation of extra-articular distal radius fractures treated with closed reduction and K-wire fixation [53]. The bone graft was delivered through a limited dorsal approach. In this series of 27 elderly patients, follow-up was limited to 16 weeks. The authors reported maintained radial height, radial inclination, and volar tilt without any adverse events, supporting the use of hydroxyapatite augmentation.

In an in vitro biomechanical study looking at the effect of CPC augmentation on extra-articular fracture models in elderly cadavers, Kainz et al. found significantly greater stiffness (59–128%) and less displacement (42–64%) in two types of volar locking plates, further supporting the use of CPC augmentation of comminuted fractures [54].

Conclusion

The spectrum of distal radius fracture patterns may make it impossible to depend on a single device for fixation, and

surgeons managing distal radius fractures should be adept at using various surgical approaches, techniques, and hardware systems. In this review, a number of relatively new implants and devices used to treat distal radius fractures were discussed. These include the intramedullary nail, intramedullary cage, radiolucent volar locking plate, distal radius hemiarthroplasty, and bone graft substitutes (Table 1). There continues to be room for improvement in the surgical management of distal radius fractures with respect to improved fixation, minimizing complications and allowing earlier motion. Additional studies demonstrating the cost-effectiveness, biomechanical properties, and clinical outcomes will be useful in determining the utility of the described techniques.

Compliance with Ethical Standards

Conflict of Interest Abdo Bachoura declares that he has no conflict of interest. Eon K. Shin declares that he serves on the Scientific Advisory Board for In2Bones.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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