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Non-Union in Upper Limb Fractures – Clinical Evaluation and Treatment Options

Paklouby u zlomenin horní končetiny – klinické zhodnocení a možnosti léčby

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SUMMARY

Although non-unions in the upper limb are rare different treatment options of this challenging situation are still affected with up to 20% of failure rate due to current literature. Risk factors for delayed and non-union of fractures are mainly the size of the fracture gap and bone loss of open fractures or in primary surgery followed by other relevant internal and external factors. In the upper limb non-unions of long bones are described with up to 30% after operative intervention. Especially in the upper limb range of motion is limited in non-union cases and disables adjacent joints like the shoulder, elbow and wrist hence reducing the total activity level of affected patients. Beside careful investigation of the causes leading to the non-union a comprehensive treatment plan should be defined to achieve successful results. Treatment can be non-operative in several, selected cases, but in the majority of cases revision surgery is necessary to achieve osseous healing.

Our own experience showed that non-union in the upper limb are rare and account for only 1.7% of all surgical managed upper limb fractures. Non-union of upper limb fractures occur most frequently in clavicle fractures followed by humeral fractures. Atrophic non-union is the most frequent reason for osseous non-union (57%) and osseous healing after revision surgery in non-unions is completed after a mean of 6.45 months.

This article will give a brief overview of the genesis, clinical evaluation, treatment options and recommendations in upper limb non-unions according to the current literature.

Key words: fracture, upper-limb, non-union, osteosynthesis, cancellous bone-graft.

INTRODUCTION

The incidence of non-union for all fractures is estimated with 5–10 % (17, 18, 33). In humeral diaphyseal fractures the non-union rate is documented with 4–10% following non-operative management and > 30% after operative fracture treatment (31, 37). Large cohort studies report an incidence of 2–10% non-union rate in forearm fractures (12, 16, 38, 39).

Osseous union is defined when complete healing of three cortices in plain radiological antero-posterior and lateral films is evident after 3 months.

If a fractured bone fails to complete osseous healing within 9 months after injury and does not show signs of callus formation within a series of plain X-rays in a 3 months period or 5 months postoperative in case of implant failure osseous non-union is present (14, 36).

Etiology

Several etiological factors are contributing to the genesis of non-union. External factors are the severity of the initial injury, comminution of fracture, soft tissue damage and conditions (open vs. closed fracture type), as well as bone loss in open fractures. Internal factors are genetic predisposition, diabetic disease, peripheral vascular disorders, cortisone therapy, mental disorders, smoking and previous skeletal injuries (8, 10, 19, 24, 27). Risk factors for the development of an infected non-union are open fracture types, open surgical revision and postoperative wound infection parallel to the mentioned contributing factors.

Fracture non-union occurs as atrophic non-union if e.g. vascular supply to the fracture zone is marginal or potent mesenchymal cells for bony union are too spare. Non-union is then due to a failure of biology as well as inadequate mechanical conditions consecutively. In the case of a hypertrophic non-union mechanical instability is the cause for non-healing of the fracture zone. Another reason for development of a non-union is infection, which will hinder the original fracture zone to heal.

Clinical and radiological assessment

For the definition of non-union in diaphyseal bone a careful clinical and radiological assessment is mandatory.

Patients with non-union will describe pain, reduced loading capacity, neurological symptoms if callus of hypertrophic non-unions will compress nerves or even the plexus brachialis. Clinical evaluation should involve documentation of the remaining range of motion. Documentation should respect clinical presentation of the arm or forearm with potential angular deformity of the affected limb, shortening of the limb and state of the soft tissues. Assessment of the vascular potential, presence of movement on stressing the non-union site and range

of motion of the above and below joints (shoulder, elbow, wrist) is necessary. Often a limited range of motion of the adjacent joints will be present due to an overall limited activity and use of the affected extremity with consecutive joint stiffness.

Plain radiographic films are necessary for documentation of the progress of fracture healing and final definition of the non-union. Further analysis of the extent of the non-union zone and evaluation of the osseous integration of the implant with CT scans is helpful for the preoperative planning and recommended if suspicion for infection exists. Radiolucent zones around implanted screws might be present. SPECT CT can be discussed in special cases when definition of non-union is unclear for detection of the non-union area. Evaluation with MRI scans might be helpful for exclusion of infection but as metalwork is often still in place artefacts may lead to false positive results.

The control of inflammatory serological blood parameters might be helpful in the detection of infected non-unions, but normal values might be present in an e.g. low – grade infectious condition. A sterile puncture or even open biopsy of the non-union zone with microbiological examination of the puncture fluid will give more exact results. Additional histopathological soft tissue evaluation will assist defining the kind of non-union.

Management

Definition of the character of non-union will guide further treatment. As an imbalance of biological and mechanical disorders lead to the development of an *atrophic non-union* surgical management should involve local debridement of the non-union zone, application of cancellous bone-graft or cortico-cancellous bone graft for improvement of local biology and improvement of mechanical stability by either change of implant or use of same implants with adapted length or thickness. The treatment concept of defined *hypertrophic non-union* is surgical excision of the hypertrophic non-union zone and improvement of stability by either change of implant or use of the same implant with adapted size in length or thickness in case of intramedullary nailing systems. In the presence of an *infected non-union* surgical management should follow a stepwise treatment with initial removal of all implants, local excision and debridement of the infected non-union zone including all avascular, necrotic tissue with extraction of biopsies for further microbiological and histopathological evaluation. Initial stability for the non-union can be achieved by placement of an external fixator. Intermittent antibiotic therapy for eradication of the defined infection has to be respected. Definite refixation of the non-union can be performed as soon as complete eradication of the infection is proved. Choose of implant is due to local osseous and soft tissue condition.

Several studies have presented their outcomes after surgical intervention following non-union with different results (1, 9, 13, 15, 26). Usually the presented concepts follow a triangular treatment concept with

1 – debridement of the non-union zone,
2 – stimulation of callus formation by adding cancellous bone graft (iliac crest), allograft or synthetic bone substitutes and
3 – improvement of the mechanical environment.

Recently the "diamond concept" has been introduced adding a fourth component to the treatment concept in non-union cases. Beside improvement of the mechanical stability, optimal vascularity to the area of interest the biological and cellular environment has to be improved by adding osteoinductive components, like cortico-cancellous bone, collagen, hydroxyapatite or recombinant growth factor, embedded in an osteoconductive scaffold (reamer irrigation aspiration (RIA)) and additive osteoprogenitor cells (Mesenchymal stem cells (MSC)) to the debrided non-union zone. A review of case series managed with this treatment scheme showed 100% success rate (15).

Nevertheless, as non-unions are specific cases with individual challenges it is difficult to define a unique treatment scheme for these heterogenic complications.

A scoring system has been presented – non-union scoring system (NUSS) – for clinical assistance in decision making for treatment of non-union (5). The factors, which are considered in this scoring system, are the bone quality, the original fracture entities (closed vs. open fracture type), number of previous interventions and adequacy of previous surgery; the bone alignment, presence of bone defect, state of the surrounding soft tissues and ASA grade (American Society of Anaesthesia). The total score of each counted factor is multiplied with 2. A total score of 0–25 points recommends a straightforward and standard treatment, 26–50 points will need more specialised care, 51–75 points require specialised care and specialised treatment, in cases with 76–100 points primary amputation of the affected limb should be considered (5).

A validation study of the NUSS by the same author group showed significant rates of union in 300 cases, which indicates that the NUSS is an appropriate scoring system to classify and stratify non-unions and enables the surgeon to choose the correct treatment (6).

Non-operative management

Non-union cases with non-operative treatment have been reported rarely. But convincing studies have shown good to satisfactory results after electric shockwave therapy, low intensity pulsed ultrasound or electro stimulation (2, 4, 11, 20, 25, 32, 41). It has to be mentioned that the patient cohort, surrounding environment and localisation of the non-union have to be carefully selected and defined for suitable non-operative treatment of non-unions.

Surgical management

Aim of every surgical intervention in orthopaedic surgery is accurate reduction and sufficient fixation to achieve bone healing. In general after definition of non-union an individual treatment concept has to be defined with regards to genesis and localisation of the underlying

case and treatment options have to be thoroughly discussed with the affected patients.

After thorough assessment of the genesis and localisation of the presenting non-union, careful decision should be made for the following treatment.

In an ***atrophic non-union*** case revision surgery with bone grafting +/- additional supplementation of osteoinductive components to the fracture zone is often described, and mandatory to improve local stability and biology.

In the situation of mechanical instability, following a ***hypertrophic non-union***, revision surgery with a change of implant including implant removal and improvement of stability with an appropriate mechanical fixation has to be considered.

When an ***infected non-union*** is present a strict stepwise and staged management should be chosen with complete implant removal, preliminary external fixation, several debridements of the fracture zone with final, definite stable fracture fixation after complete eradication of the infection. Immediately after perioperative collection of biopsies of the non-union area an empiric antibiotic therapy should be started intraoperatively (most commonly with an agent of the cephalosporine group) adapted to a specific antibiotic after definite analysis of the microbiology and tested antibiotics.

In extremely challenging cases of osseous non-union and several failed management approaches the local application of rh-BMP-2 (InductOS®) to the excised non-union area and supplemented cancellous bone showed satisfying to good results with complete osseous healing in 76% as per report of a study of 25 patients reviewed over 18 months (35).

Shoulder and upper arm

Clavicle

For surgical treatment of non-unions of the clavicle shaft and medial portion the use of an angular stable implant is recommended after complete implant removal, excision of the non-union area and if necessary application of autologous cancellous bone graft or a cortical iliac crest graft to maintain the length of the clavicle. By experience the use of pre-contoured and pre-bended 3.5 mm reconstruction plates are recommended for management of clavicle shaft non-unions (case 1). Initial fracture reduction and fixation of clavicle shaft fractures using an intramedullary fixation device (e.g. TEN / ESIN (elastic – stable intramedullary nailing system)) has gained attention in the last years for a satisfactory fracture alignment but cannot be recommended for the stabilisation of non-unions because of lacking stability. Hence potential development of a hypertrophic non-union is risked. In the presence of non-union of the lateral clavicle 2.4 or 2.7 mm mini fragment plates can be utilized for revision surgery either in a single fixation method, or as just recently favoured in a double fixation method by placing one plate anteriorly and the second one posteriorly. If there is an additional injury of the coraco-clavicle and/or acromio-clavicle ligaments, an additional coraco-clavicular and/or acromio-clavicular stabilisation seems to be necessary. The hook plate is a commonly used implant in these conditions. Adverse effects like pain-syndromes and/or osteolysis of the acromion around the hook are reported. Therefore early implant removal, as soon as bony healing is documented, is necessary in order to minimize these problems. Alternatively, recent implant developments include the option of a coraco-clavicular suture fixation (tightrope equivalent / suture anchor) through the eyelet of dedicated, pre-contoured lateral clavicle plates. Additional temporary transfixation of the acromio-clavicle joint using K-wires is not recommended, since an early implant migration can be seen frequently.

Depending on the character of the non-union decortication of the non-union area should be made first in hypertrophic non-unions, in atrophic non-unions application of autologous cancellous bone graft should be performed. In large defect zones the implantation of a cortical iliac crest graft to maintain the length of the clavicle should be considered. In these cases, a thorough preoperative planning using X-rays of the contralateral clavicle for estimating the appropriate length is mandatory.

Humerus

Subcapital non-unions of the humerus are rare, indication for revision of the non-union is pain, limited range-of-motion and reduced loading capacity.

The classic deltoideo-pectoral approach offers a good overview and can be easily extended proximally and distally. In proximal humeral fractures restoration of the medial calcar is necessary followed by restoration of the humeral height. Malreduction fixed in a varus position may lead to failure of fixation and limited range of motion. Overall the management of non-unions of the humeral bone has to respect patient's age and character of the implant *in situ* (Case 2).

In general complete removal of the material and thorough debridement of the non-union area has to be per-

Fig. 1. Case 1: 16-year-old male patient presenting with an aseptic non-union of the lateral clavicle after nonsurgical management. Treatment was by excision of the non-union zone, application of cancellous bone graft and placement of 3.5mm reconstruction plate. Complete osseous healing was present 2 months later.

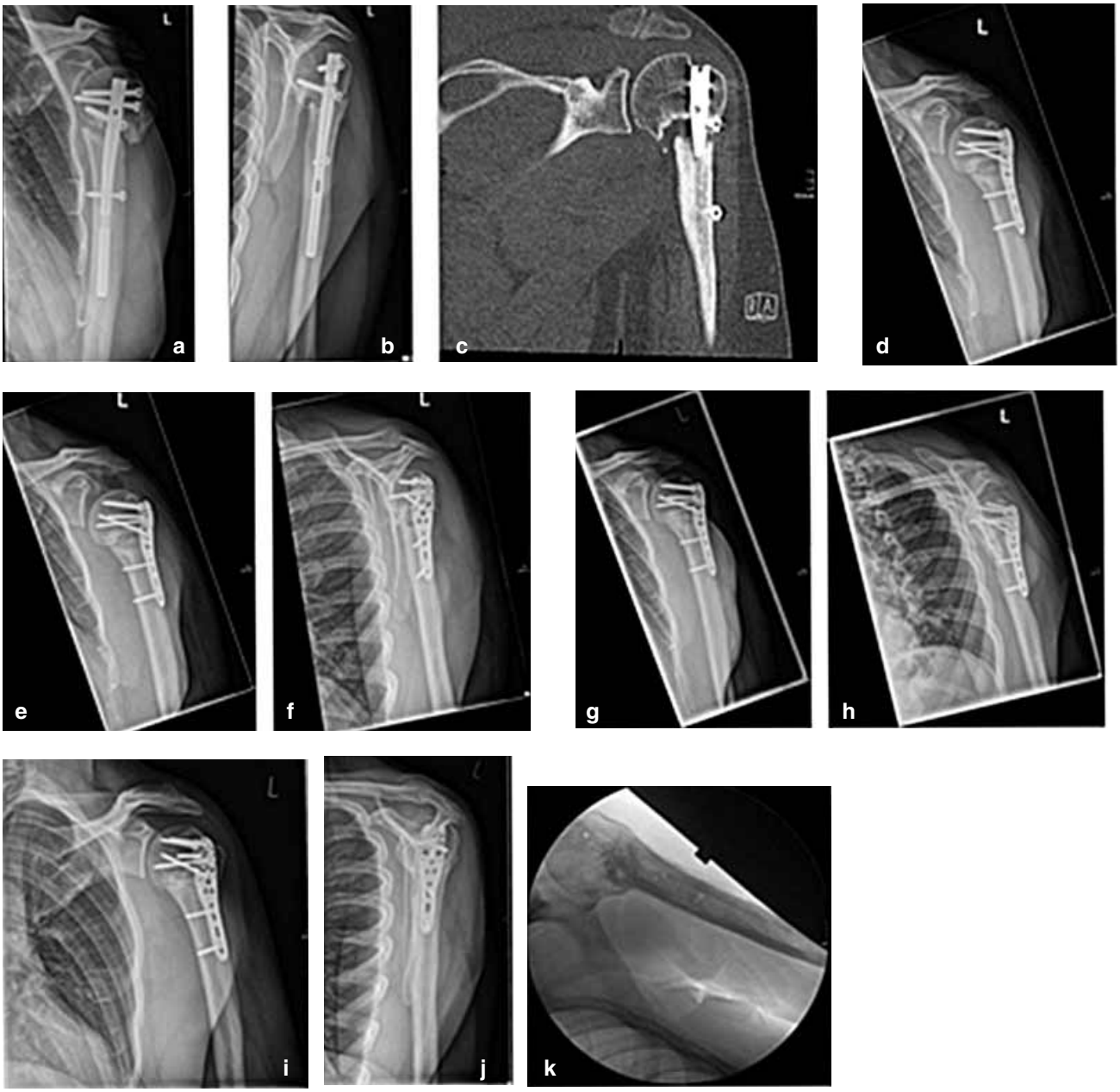

Fig. 2. Case 2: 55-year-old gentleman who was presenting with capacity restraint pain of the left arm due to a non-union of the proximal humerus 2 years after surgical intervention following a 2-part humeral head fracture managed with proximal humeral nail (PHN). After sequesterotomy of the non-union, corrective valgus osteotomy and refixation with a angular locking plate (Philos plare) complete osseous union was achieved 6 months after surgical revision of the non-union. Implant removal was performed 2 years after revision surgery.

formed initially before further surgical intervention. If a joint preserving approach is chosen, the reduction of the proximal humeral non-union follows the concepts of initial fracture reduction. It is of special interest, to restore the calcar anatomically to avoid any non-anatomical position of the humeral head (i.e. varus – or valgus – deformity and/or posterior tilt of the humeral head). In some cases, it might be beneficial to impact the humeral shaft in the humeral head in order to gain more bone contact and stability. Alternatively, bone grafting using a "competent" bone block (i.e. allograft of the femoral head, fibula graft) might be considered.

Nowadays the consequent fixation of the proximal humerus is achieved with pre-shaped locking plates for the treatment of non-unions (e.g. PHILOS Plate (proximal humeral internal locking system)). In elderly patients the implantation of a total joint replacement (anatomic prosthesis vs. inverse prosthesis) has a relevant significance, whereby a trend towards implantation of inverse shoulder prosthesis can be observed.

In non-unions of the humeral shaft the use of a narrow 4.5 mm LCP (locking compression plate) is recommended, during preparation special attention to the radial nerve should be given. The size of the LCP should be long

enough, pre-bending might be helpful to achieve higher compression, and as this implant should function as an internal fixator placement of the screws should be performed responsively. If intended additional compression of the interfragmentary zone can be achieved by excentric implantation of the screws or with a plate spanner. Alternatively intramedullary nailing systems are commonly used. Surgical management of the humeral non-union can be achieved by reaming the medullary cavity and exchanging the intramedullary nailing device to a bigger one in diameter and length. Compression of the interfragmentary zone can be achieved by placing the distal locking screw first, hitting back the intramedullary nail and insertion of the proximal locking screw secondly, optional some implants like the unreamed humeral nail (UHN) provide a compression device to achieve this. Compression of the intramedullary nail is helpful in simple oblique and transverse fracture types but is contraindicated in spiral, long oblique and instable fracture types.

For management of supra-, per- or diacondylar humeral non-unions a dorsal approach to the distal humerus should be made with either a longitudinal incision of the triceps tendon or a paratriceps approach. The dorsal approach can be easily extended distally following the olecranon and ulnar shaft. A 3.5 mm reconstruction plate, in individual cases a narrow 4.5 mm LCP is the most suitable implant to be used in non-unions of the distal humeral part. Newer plate designs of pre-contoured 3.5 mm angular locking plates (e.g. radial and ulnar distal humerus plate) with placement of variable angle locking screws allow for elegant and minimal invasive management of distal humeral non-unions. In elderly patients aged 75 years and older the implantation of a total joint replacement in distal humeral non-unions should be carefully assessed and discussed.

In a retrospective review study of 35 humeral non--unions 8 infected non-unions were managed in a 2 staged procedure with Ilizarov frame followed by compression plating, 23 patients with non-union without infection were treated in a 1-staged procedure with plating and cancellous bone graft and 4 non-unions in osteoporotic bone were managed with fibular strut grafting for additional stability (26). Results after median follow-up of 16 months showed a median union time after 6.5 months with best results in the group of one-staged compression plating procedure (26).

These results are in agreement with other studies showing that compression plating enables correction of axis, malalignment, stimulation of osteoporosis with a union rate of 83–100% (5, 6) and 92–100% with additional autologous cancellous bone grafting (22, 29, 30, 34).

There are limitations for treatment of non-unions with plating like osteoporotic bone structure, disuse of the implant or previous surgery (1, 28) hence management of non-unions of the humeral shaft with intramedullary nailing systems have shown satisfactory results (7, 13, 23, 40). Compared with plating even better outcomes have been reported with intramedullary nailing devices (13, 23, 40). For achievement of interfragmentary compression newer implant designs allow for improved compression of the debrided non-union zone with nailing systems (e.g. UHN) nowadays. In a retrospective study of 51 patients treated with retrograde humeral nail for aseptic non-union of the humeral shaft 94% union was reported after a median healing time of 10.1 months (3).

Forearm

Olecranon

Non-unions of the olecranon should be isolated from proximal ulna non-unions by definition of the former fracture line. Again complete removal of the inlaying implant is necessary followed by careful debridement of the non-union zone +/- apposition of autologous can-

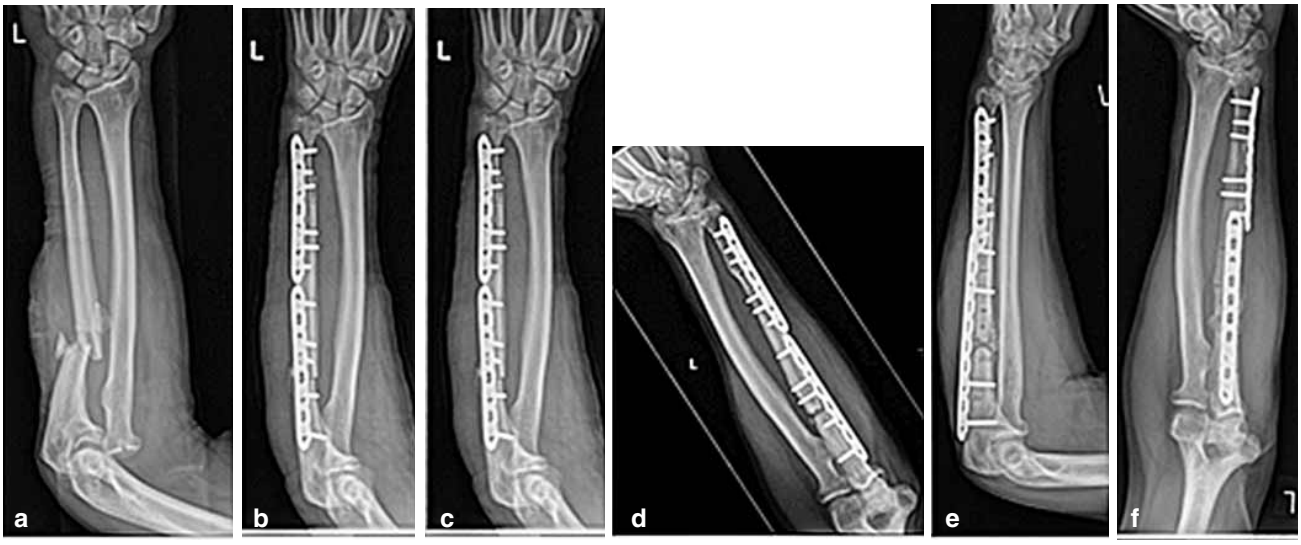

Fig. 3. Case 3: Monteggia fracture of a 55-year-old male patient, fixed with 3.5mm LCP initially, after establishment of an aseptic non-union he underwent revion surgery with placement of cancellous bone graft, BMP and compression plating. Callus formation was visible 12 weeks after revision surgery.

cellous bone graft. Anatomic reduction is mandatory to avoid or reduce the risk of posttraumatic arthrosis. Definite fixation is achieved by placement of angular stable plating systems, which have been introduced lately (e.g. 3.5 LCP Olecranon locking plate). The commonly used tension band fixation of the olecranon is not recommended in these cases, since lacking of the required stability is biomechanically proven.

Ulna and radius

Treatment of non-unions of the forearm does not differ from the management of radial or ulnar shaft fractures (Case 3). Anatomical approach to the radius is achieved following a longitudinal incision between the radius styloid process to the radial epicondyle and careful approach to the radius between the extensor digitorum and extensor carpi radialis brevis muscle. Attention has to be made to the course of the radial nerve. Ulnar incision is following the anatomic bony formation and approach between the extensor carpi ulnaris and extensor digiti minimi muscles, which are retracted dorsally, and anconeus muscle and flexor carpi ulnaris muscle on the volar side. A 3.5 mm DCP (dynamic compression plate) or LCP can be used in hypertrophic non-unions and after excision of the non-union +/- apposition of autologous cancellous bone graft in atrophic non-unions. The use of a plate compression device is helpful for achievement of interfragmentary compression. In the very rare case of a non-union in the distal radius management should be using a volar radial 2.4 LCP or angular locking plate as well with the optional use of variable angle locking screws.

In a Dutch retrospective series with a long-term period of 33 years review 47 patients with 51 forearm non-unions median healing time to complete union after revision surgery was achieved after 7 months (21). 59% cases were managed with compression plating and additional autologous cancellous bone graft, 27% with compression plating alone and in 14% only bone graft was used. The study showed 100% osseous healing but 13% complication rate (refracture, wrist stiffness, nerve injury and infection).

Complications

Beside general operative risk factors with potential complication rate like bleeding, haematoma, infection etc., re-fracture of the revised non-union, wrist stiffness especially in non-union of radius and / or ulna diaphysis and synostosis in forearm non-union are known (21). For the humeral shaft postoperative nerve injury, especially radial nerve palsy, which is seen in 18% in closed fractures – most common in middle third humeral shaft fractures – are described. Long-term functional outcome might be disappointing in approximately 20% of the cases (21).

Retrospective analysis

In a retrospective, radiographic study all charts of patients treated for upper limb fractures, resulting from a mono-trauma, were reviewed by the main author. Data selection was made using the ICD (International Classification of diseases) coding system. The period of analysis was between January 1st 2014 to December 31st 2015 to allow a reliable, radiographic follow-up documentation. Exclusion criteria were incomplete radiological documentation or patient charts, as well as polytraumatized patients. No clinical follow-up was made for this data analysis.

The 24 months retrospective, radiographic review of upper limb non-unions treated in our clinic revealed 21 non-unions (1.7%) in upper limb regions out of a total of 1,192 surgical managed upper limb fractures. Non-union was defined 6 months after surgical intervention with no evidence of callus formation in plain radiographic films. We had 12 non-unions in clavicle fractures out of 210 surgical treated clavicle fractures during this period (6.1%). In 4 cases non-union was seen after non-operative management, 3 patients showed non-union due to postoperative infection and in 5 cases no callus formation was found after surgical management of clavicle fractures with plate osteosynthesis.

5 patients out of a cohort of 344 surgical managed humeral fractures showed non-union (1.4%) with hypertrophic non-union after non-operative management in 2 cases and evidence of an atrophic non-union following plate fixation of humeral fractures in 3 cases.

In the forearm we had 4 non-unions out of a total of 638 surgical treated forearm fractures (0.6%). 2 patients showed hypertrophic non-union after plate fixation of an ulna fracture, 1 atrophic and 1 hypertrophic non-union was evident after surgical management of a proximal radius fracture (Table 1).

Table 1. Overwiew of the allocation of non-union types in surgical treated upper limb fractures

Upper Limb Region													
Type of	Clavicle			Humerus			Radius			Ulna			Total
Non-union	medial	shat	lateral	proximal	shat	distal	proximal	shat	distal	proximal	shat	distal	
atrophic	0	2	2	1	1	1	1	0	0	0	0	0	n = 12 (57 %)
hypertrophic	0	3	2	0	2	0	1	0	0	1	1	0	n = 5 (24 %)
infected	0	2	1	0	0	0	0	0	0	0	0	0	n = 4 (19 %)
Total	0	7	5	1	3	1	2	0	0	1	1	0	n = 21

Overall atrophic non-unions were verified in 12 cases (57.14%), hypertrophic non-union in 23.8% (n = 5 out of 21 non-unions). Non-unions due to postoperative infection were found in 4 cases (19%) (Table 1). 2 out of the 12 patients with atrophic non-unions showed pathologic, atrophic fracture non-unions suffering mamma carcinoma and synovial sarcoma respectively.

In two patients fracture non-union was managed by total joint replacement of the elbow (non-union of the distal humerus and radial head) and one patient underwent radial head resection due to an atrophic non-union of the radial neck.

Complete osseous healing was seen after a mean of 6.45 months (3–12 months) after surgical revision of the non-union.

Our numbers and period of retrospective follow-up is small, but osseous healing outcome is in agreement with larger cohort studies (26). The clavicle appears to be affected most frequently with osseous non-healing, independent whether the fracture location is laterally or in the medial third and whether initial management was non-operative or surgical.

CONCLUSIONS

Definition of an osseous non-union is made by radiological assessment after a period of 4–6 months after initial surgery. Our own numbers revealed that non-union in upper limb fractures account for only 1.7% and are frequently seen after clavicle fractures. Although the incidence of non-union might appear low assessment and management can be challenging and extended. Beside a careful investigation a constructive conversation with the patient and family members for achievement of a both sided satisfying result is recommendable.

There are a couple of principles, which should be considered in the treatment plan:

- Debridement of avascular tissues in atrophic non-unions.
- Eradication of infected non-union areas and course of antibiotics.
- Complete removal of failed implants.
- Restoration of alignment, length and rotation of the affected limb.
- Stable fixation using compression plates.
- Optimization of a bone-forming environment (bone graft etc.).
- Additive treatment of osteoporosis.

Currently the gold standard in revision surgery of diaphyseal non-unions is the use of a compression plate or an angular locking plate as a bridging plate, used as an internal fixator, and placement of cancellous bone graft. If the non-union is located epiphyseal or even intraarticular (e.g. Olecranon fractures) surgical management has to be adapted and modern plate designs can be discussed for revision surgery or complete excision of the non-union area with the adjacent proximal or distal end of the affected bone. In selected cases partial to total joint replacement is a considerable surgical solution.

We recommend a careful analysis, design of a treatment plan and stepwise management in case of infected non-unions including temporal external fixator treatment and a course of specific antibiotics before re-fixation of the affected long bone.

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