



Nonunion of the radial neck in children: a rare but severe complication after fractures of the radial neck

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Received: 18 October 2020 / Accepted: 6 January 2021 / Published online: 3 March 2021
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Abstract

Purpose Nonunion of the radial neck poses an enormous challenge for treating surgeons. It is a very rare complication of the radial neck with limited experiences. In this current major study, the authors report of their own experiences concerning this problem.

Methods 11 patients with severe displaced radial neck fracture Metaizeau type IV with elbow dislocation and 2 ongoing fractures. 9 fractures had to be treated with open reduction, six with intramedullary nailing, two with K-wires and one with periosteal suture fixation. In two children, aged 4 and 5, the fracture was not diagnosed initially. The patients showed a successful reduction intraoperatively.

Results All patients developed nonunion of the radial neck. 9 out of 11 children presented with pain and 5 out of 11 with valgus deformity. All children underwent surgical management of the complications. 3 children received a debridement of the elbow joint with resection of the fragmented radial head. 7 cases needed a following reduction, spongiosa-plasty and periosteal flap reconstruction and plate osteosynthesis. One patient received radial intramedullary pinning. All nonunions showed reunion. All patients with obtained radial head showed significant improvement concerning complaints and range of motion. Only one child showed a slight deterioration in range of motion. Children with resected radial head showed good range of motion but complaints and instability in loaded joint needing further surgical treatment.

Conclusion Treatment of radial neck nonunion in children should not be delayed until pain, deformity and limited function occurs because this goes along with severe transition of the radial head right up to bone atrophy.

Keywords Nonunion of radial neck · Radial neck fractures · Children · Complications

Introduction

Radial neck fracture accounts for 4.5–21% of the pediatric elbow fractures [1–3]. Most of these fractures are minimally displaced and suitable for conservative treatment. Especially, young patients with a dislocation less than 30° show very good results [4].

Higher grades of dislocation of the radial neck fractures usually need surgical treatment and are associated with a higher rate of complications. Clinical complications are recorded as limited range of motion with or without pain, cubitus valgus and crepitation. Radiological signs show diverse variances from dislocation ad latus to severe

deformity of the head, proximal radioulnar synostosis, heterotopic ossification, avascular necrosis and nonunion of the radial neck [1, 3, 5]. Radial neck nonunion counts as a rare but severe complication. Even large studies showed poor results in up to 30% but without mentioning nonunion as a reason [6–8]. There is a lack of experience in dealing with radial neck nonunion. Research brought up only one study with nine patients [5] along with several case reports [2, 9–11], clarifying the complexity of this rare complication along with radial neck fracture.

This article is a retrospective analysis of 11 cases of nonunion of the radial neck fracture in children.

The aim of this report is to review the course after displaced radial neck fracture along with different treatment options.

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Methods

Clinical charts of 11 children with nonunion of the radial neck were reviewed by mechanism of injury, concomitant elbow injury, way of primary surgical treatment and postoperative complications. Radiographic evaluation documented fracture geometry, degree of angulation, percentage of dislocation ad latus and concomitant injuries at time of accident. Postoperative radiographic series were screened to quality of reduction and type of surgical procedure. Especially existent intraoperative and early complications were recorded (Tables 1, 2).

Further radiographs while follow-up were investigated for the development of nonunion.

All patients were screened for radiological angulation of the radial neck and substance defect in radial neck or head. Development of nonunion of the radial neck was recorded. During follow-up process of the radial head was assessed including head deformity, position in the radiohumeral joint, avascular necrosis, radioulnar synostosis, heterotopic ossification, premature closure of growth plate and secondary deformity.

Cubitus valgus, function of elbow and forearm and clinical complaints were reported during follow up.

Table 1 Patient demographics and injury information

Pat id	Sex	Side	Age at injury (year)	Associated injuries	Fracture type	Initial Angulation of fracture (degree)	Percent and direction of translation	Maitezeau -Classification	Bony contact / no bony contact
1	M	Right	14	Elbow dislocation	Salter II	80	100	Maitezeau IV	Bony contact
2	M	Left	11	Elbow dislocation	Salter II	92	100	Maitezeau IV	No bony contact
3	F	Left	12	Ellenbogenluxation/humerus head fracture	Salter II	90	100	Maitezeau IV	No bony contact
4	F	Left	7	Elbow dislocation	Salter II	90	100	Maitezeau IV	No bony contact
5	M	Left	10	Elbow dislocation/coroneuoidesus	Salter II	70	80	Maitezeau IV	Bony contact
6	M	Left	10	Elbow dislocation	Salter II	90	100	Maitezeau IV	No bony contact
7	M	Right	8	Elbow dislocation	Salter II	70	100	Maitezeau IV	No bony contact
8	M	Left	5	Elbow subdislocation	Salter II	90	100	Maiteteau IV	No bony contact
9	F	Left	10	Elbow dislocation	Salter II	70	80	Maitezeau IV	Bony contact
10	F	Right	8	Elbow dislocation	Salter II	80	100	Maitezeau IV	Bony contact
11	M	Left	4	Elbow subdislocation	Salter II	90	100	Maitezeau IV	No bony contact

Table 2 Initial treatment of radial neck fracture

Pat id	Initial treatment	Postoperative radiograph: residual dislocation (degrees)	Early complications (1–30 Days postoperative)	Remove metal
1	ORIF/ESIN	0	Loss of reduction/migration of ESIN	6 Weeks
2	ORIF/ESIN	0	None	3 Months
3	ORIF/ESIN	0	Loss of reduction	4 Months
4	Periosteal suture	20	Loss of reduction	None
5	ORIF/ESIN/anchor proc Coroneuoidesus	0	Migration of ESIN	4 Months
6	ORIF/ESIN	0	Migration of ESIN	3 Months
7	ORIF/K-Wire	0	Correction loss/additional ESIN	3 Months
8	Dismissed	Overlooked	Overlooked	Overlooked
9	ORIF/K-Wire	0	Loss of reduction	6 Weeks
10	ORIF/ESIN	0	Pain in extension and flexion of fingers	6 Weeks
11	Dismissed	Overlooked	Overlooked	Overlooked

Results

There were 11 cases, 4 girls and 7 boys, with ages ranging from 4 to 14 years and an average of 9.2 years at time of injury. 3 children were seen in our hospital initially, and we saw eight children with known nonunion of the radial neck after surgical treatment for further therapy. The left arm was involved in eight cases; the right arm in three cases. 10 cases showed an isolated injury of the elbow, one case a concomitant fracture of the humeral head. Associated elbow dislocation was observed in nine cases and subluxation of the elbow in two cases. 2 patients revealed a concomitant bone injury of the elbow.

All fractures of the radial neck were classified as Salter–Harris type II fractures. Evaluating according to the modified Metaizeau classification, all 11 cases showed severe dislocation with more than 60° of epiphyseal tilt, accordingly Metaizeau grade IV. An angulation, defined by the angle between a perpendicular line to the articular surface and the radial shaft in a.p. X-ray, of mean 84° degree (range 70°–90°) was observed.

In addition, we examined the contact of the radial neck to the metaphysis classified by Kaiser [8] (contact/no contact) to assess the extent of dislocation. In four children, contact could be proven between the radial neck and metaphysis; seven cases had no contact.

In three children, fracture was missed initially. A 10-year-old girl with initial dislocation and reposition showed a posterior displaced radial head 2 days later. In two children aged 4 and 5, radial neck fracture was not identified because the bony nucleus was not visible yet.

Primary treatment

A closed reduction was unsuccessfully attempted in all of the primarily operated children, and the radial head was thereafter openly reduced. In six cases, the radial neck fracture was treated with elastic stable intramedullary nailing, in two cases with K-wire and in one case with periosteal suture at the radial neck. In one case, a posterior displacement of the radial head was diagnosed 2 days after unsuccessful closed reduction and open reduction with intramedullary nailing took place. 2 children with missed fracture received conservative treatment with immobilization.

In one child, early loss of reduction was seen two days after open reduction along with K-wire fixation treated with additional intramedullary pinning.

Intraoperative and postoperative radiographs showed a successful reduction of the radial head in eight cases. One child showed residual angulation of 20° which was accepted.

In seven children, early complication like loss of reduction and dislocation of ESIN occurred. In one case, irritation of M. extensor pollicis longus tendon leads to a removal of the nail 6 weeks after surgical treatment. Removing surgery took place in between 6 and 16 weeks postoperatively.

Clinical and radiological findings at presentation

The indication of revision surgery was required 14 weeks–5 months after primary surgery in the 3 children with primary treatment at our hospital. The 4-year-old boy with missed radial neck fracture presented 36 months after injury. The other nine children consulted us 10 months–7 years after primary treatment (Table 3). 9 out of 11 children presented with pain, 2 children did not experience pain. All children showed crepitation of the elbow while pronation–supination. Loss of pronation–supination was present in all cases affecting both pronation and supination.

Reduction of flexion–extension of the elbow was seen in 10 out of 11 children. Only one child showed no limitation of elbow motion within the sagittal plane. 5 out of 11 children presented with cubitus valgus range from 10° to 25°.

Radiographic findings showed a severe fragmented radial head in three children. Therefore, three children had developed significant changes of the capitulum humeri with radiological provable lines. In these three children, injury was dated back 11 months, 4 and 7 years. 3 children presented between 2.5 and 5 months after injury without radiological changes despite nonunion and heterotopic ossification as confirmed by X-ray and MRI. In five children, we noted massive changes of the radial neck and head as well as displacement in diverse planes (Fig. 1).

Surgical treatment

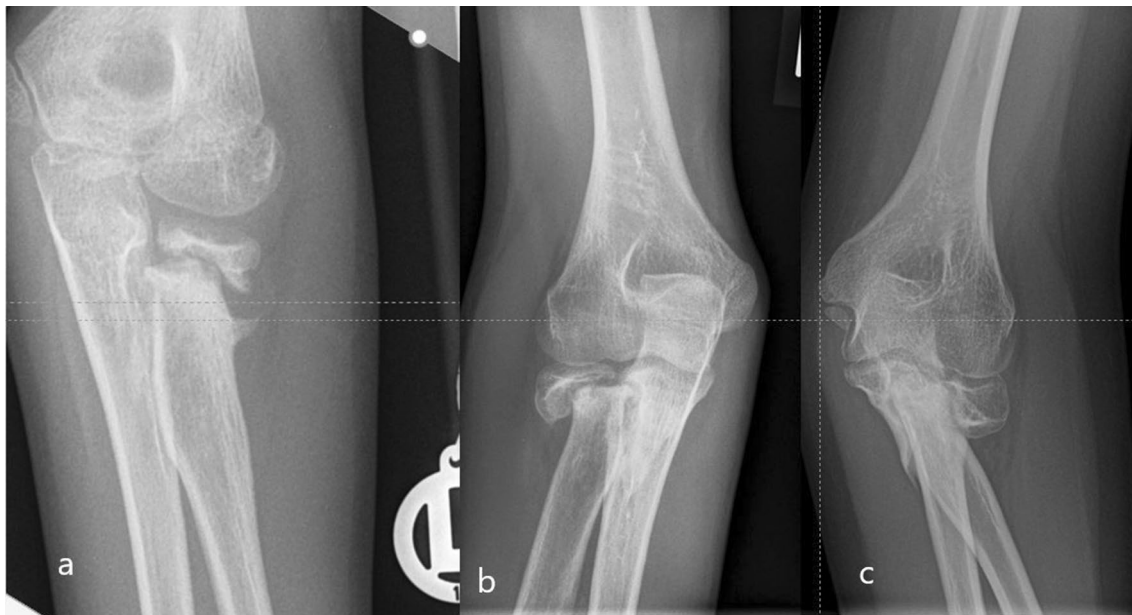
Indication for surgical treatment was determined by pain, functional disability, limited range of motion and radiographic changes. The aim of surgical procedure was releasing pain, increasing range of motion, reconstructing the radiohumeral joint and preventing further deterioration of the elbow. Even the two of three children with fragmentation of the radial head were treated with the intention to retain the head.

Originated defects of the radial neck and head were classified into four types (Table 4). 3 children were found to have no defects of the radial neck or head (case 5, 8 and 11). 4 of children presented with massive defects of the radial neck and head. Two of these even showed a fracture and dislocation of the metaphysis through the radial head (Fig. 2). 3 children showed a massive dissolved radial head in diverse parts, consequently unsuitable for 'on the table

Table 3 Clinical and radiological outcomes by time of surgical indication

Pat id	Time between injury and presentation for non-union	Clinical presentation	Range of motion (pronation/supination extension/flexion)	Arm axis	Percent persistent lateral (L) and/or anterior (A) translation (%)	Additional radiologic complications
1	10 months	Pain, Loss of rotation	60/0/10 0/0/130	IOS	L:50% and A 10%	NU, RHE, RHD, DCRU
2	11 months	Pain, loss of rotation	70/0/50 0/10/130	Valgus Deformity 10°	L: none A: 10%	NU, RHE, DCRU, RHD
3	11 months	Painloss of rotation	70/0/70/ 0/20/130	Valgus Deformity 20°	Resolved radius head	AVN,FR,HO, DCRU
4	11 months	No pain, loss of rotation	80/0/80/ 0/0/140	OS	L 50% and A: 90%	NU, RHE, RHD, DCRU
5	5 months	No pain, loss of rotation	20/0/0 0/30/100	Valgus Deformity 10°	L:20% and A: 20%	NU;HO
6	3, 5 months Wochen	Pain, loss of rotation	40/0/80/ 0/10/130	IOS	L:40% and A: 10%	NU;HO
7	7 Jahre	Pain, loss of rotation	20/0/30 0/30/120	Valgus Deformity 10°	Resolved radius head	AVN, RHE, UC
8	2, 5 months	Pain, loss of rotation	30/0/10/ 0/60/100	IOS	Dislocated radial head	NU
9	4 Years	Pain, loss of rotation	40/0/20 0/20/130	Valgus Deformity 25°	Resolved radius head	AVN, FR, UC
10	11 months	Pain, loss of rotation	50/0/5 0/20/110	IOS	L 50% and A: 40%	NU, RHE,FR, SRH
11	35 months	Pain, loss of rotation	80/0/30 0/20/130	IOS	Dislocated radial head	NU, RHE, DCRU

NU nonunion, AVN avascular necrosis of the radial head, FR fragmented radius head, RHE radial head enlargement, HO heterotopic ossification, SRH: subluxation of radial head, IOS Identical to the opposite side, RHD radius head defect, UC usures in capitulum humeri, DCRU degenerative change of radioulnar joint

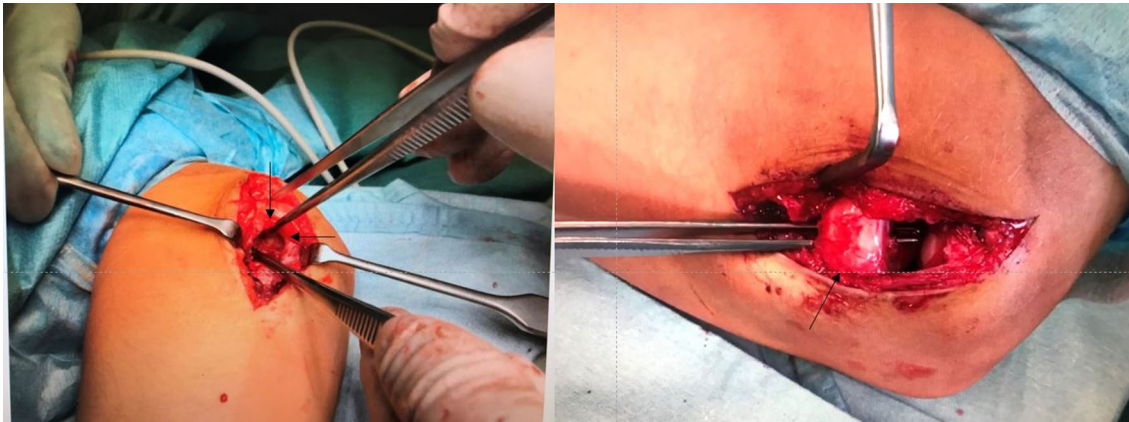
**Fig. 1** a–c X-rays of patient at initial presentation; **a** case 1; **b** case 2; **c** case 10

reconstruction'. Fixed adhesion could be seen in 9 out of 11 patients. Case number 11 revealed a radial neck fixated lateral at the metaphysis being displaced for 35 months.

The deformity was that pronounced with undermined head that spongiosa-plasty was needed to reach stability with an angle-stable plate osteosynthesis.

Table 4 Intraoperative results of surgical procedure

Pat id	Defekte RADIUSKOPF Typ I: kein Defekt Typ II: Defekt < 50% Typ III: Defekt > 50% Typ IV: Kopfmehrfragmentiert	Condition of radial head Perforated/fragmented/none	Adhesion	Surgery	Complication
1	Typ III	Perforated radial head	Present	Spongiosa-plasty, plate osteosynthesis	None
2	Typ III	None	Preent	Spongiosa-plasty, plate osteosynthesis	None
3	Typ IV	Fragmented	Present	Removal of fragments	None
4	Typ III	None	Present	Spongiosa-plasty, plate osteosynthesis	None
5	Typ I	None	None	Spongiosa-plasty, plate osteosynthesis	None
6	Typ II	None	None	Spongiosa-plasty, plate osteosynthesis	None
7	Typ IV	Fragmented	Present	Removal of fragments	None
8	Typ I	None	None	Reduction, ESIN	None
9	Typ IV	Fragmented	Present	Removal of fragments	None
10	Typ III	Perforated radial head	Present	Spongiosa-plasty, plate osteosynthesis	None
11	Typ I	Narrow radial head	Present	Spongiosa-plasty, plate osteosynthesis	Posterior displacement of the radius head

**Fig. 2** Trituration of the radial neck and head by the metaphysis with massive defect zone. The forceps passes the defect in the neck and head to proximally

Results

Children with resection of the fragmented dissolved radial head

The three children (cases 3, 7 and 9) were followed up 29, 35 and 38 months after initial surgery. All children showed increase in range of motion after surgical treatment. As it can be seen in Tables 3 and 5, the surgical procedure improved significantly in particular forearm

turning movements. Instability was complained of all three patients. The cubitus valgus was still present. 2 children followed a surgical stabilization with interpositionplasty leading to distinct improvement of subjective stability of the elbow joint. One patient with 25° cubitus valgus received varus Dome Osteotomy leading as well to improvement of stability. Another patient (case 3) needed a stabilizing elbow orthosis. Elbow valgus angle was measured by 20°. Explanatory meeting and a risk assessment was held with this patient but no further surgical treatment required (Fig. 3).

Table 5 Clinical and radiological follow-up

Pat id	Bones consolidation	Range of motion (pronation/supination/extension/flexion)	Mayo elbow performance score	Reoperationen	Arm axis	Personal assessment: dissatisfied, satisfied, very satisfied	Follow up
1	Yes	70/0/20/ 0/0/130	100	No	IOS	Satisfied	22 months
2	Yes	80/0/20 0/0/130	100	No	Valgus deformity 10°	Very satisfied	36 months
3	Resection	90/0/90/ 0/0/140	60	No	Valgus deformity 20°	Dissatisfied	29 months
4	Yes	70/0/20 0/0/140	100	No	OS	Very satisfied	10 months
5	Yes	70/0/30 0/0/130	100	No	Valgus deformity 10°	Very satisfied	14 months
6	Yes	45/0/90 0/5/140	100	No	IOS	Very satisfied	26 months
7	Resection	80/0/20 0/20/130	70	Interposition plastic	Valgus deformity 10°	Satisfied	38 months
8	Yes	80/0/90 0/0/140	100	No	IOS	Very satisfied	36 months
9	Resection	70/0/80 0/0/130	60	Dome osteotomy	Valgus deformity 5°	Satisfied	35 months
10	Yes	80/0/70 0/0/140	100	No	IOS	Very satisfied	58 months
11	Yes	30/0/10 0/5/130	80	TSF	IOS	Satisfied	120 months

Mayo Elbow Performance Score revealed poor results between 60 and 70 points for these children.

Subjective evaluation categorized two children not satisfied and one patient satisfied with postoperative result.

Children with maintenance of the radial head

All children (cases 1, 2, 4, 5, 6, 8, 10, 11) were followed up for a mean of 40 months (2–120 months). All surgical treatments with maintenance of the radial head lead to bone union of the nonunion.

7 of 8 children demonstrated significant improvement in range of motion of the elbow and forearm pronation–supination (Tables 3, 4). One girl (case 4) revealed reduction of pronation and supination, particularly supination. According to freedom of symptoms, she was quite content.

7 out of 8 patients needed no further surgical treatment except removal of osteosynthesis material. All children underwent implant removal. Case 11 showed a posterior displacement of the radial head following revision surgery with Taylor Spatial Frame (TSF). Recurrent subluxation occurred after TSF treatment. Subjective evaluation classified six children very satisfied and two cases satisfied. 7 out of 8 children reached 100 points (excellent result) in Mayo Elbow Performance Score, one child 80 points (good result).

Discussion

As radial neck fractures in children represent 10% of bone injuries of the elbow, they count for common fracture. One rarely seen complication is the radial neck nonunion. Review of literature identified few case reports [1, 3, 9]. Only one case series, including nine children, describes radial neck nonunion along with therapy [5]. Because of the unique anatomic structure of the radial neck and head with the exclusive blood supply of the radial head from the metaphysis, the rate of nonunion of the radial neck after severe displaced radial neck fractures or complicated elbow joint displacement would expected to be higher. A high-energy trauma with avulsion of the radial neck could be leading to destroyed vascular structures. Surgical manipulation can increase the impairment of the soft tissue and blood supply [12]. However this is a controversial discussed issue [8, 13, 14]. De Mattos et al. [13] reviewed over 193 children with radial neck fracture of whom 13% underwent surgical treatment. The authors observed open reduction to be associated with worse results. Higher fracture angulation and concomitant injuries were not related. Kaiser et al. analyzed 19 children with Judet type IV with and without bony contact between the radial head and the

Fig. 3 Course of patient case 10: **a** X-rays at presentation 11 months after accident with severe defect of the radial head and neck; **b** CT and MRI imaging of the defect zones; **c** intraoperative X-rays after periosteal flap reconstruction, spongiosa-plasty of iliac crest and stabilization with angle-stable plate-osteosynthesis; **d** and **e** course of the bony consolidation of the radial neck and remodeling of the radial neck and head; **f** bone union of the nonunion with good quality of reduction. Anatomical position of the radial head along with good ranges of motion in the elbow

radial neck. They found the extent of displacement to be the main cause for poor results, whether an open reduction took place or not. Gutierrez et al. came to a contrary opinion and believed that there was no statistically significant association between the type of surgery and the definitive Mayo Performance Elbow Score (MEPS) noted [14]. However, a statistical significant association was found between the initial radial head dislocation and the final MEPS.

The rate of nonunion, as to be rarely described in literature, and the rate of heavily displaced radial neck fractures Metaizeau type III or IV vary significantly, regardless of whether open reduction or severe displacement is counting for poor results [2, 6–8, 14].

We analyzed 11 cases of only heavily displaced radial head Metaizeau type IV fractures. 9 patients had a previous unsuccessful closed reduction with subsequent open reduction. In 2 out of 11 patients, fracture was dismissed.

Open reduction is a more invasive intervention as soft tissue and the blood supply of the radial head additionally are compromised. Therefore risk for avascular necrosis and nonunion increases [1, 2, 12, 15].

It is recognized that the results of intramedullary nailing differ distinctly from the ones before the period of intramedullary pinning observed by up to 45% poor functional outcomes [2, 7, 15].

Nevertheless, five of seven children with treatment of ESIN showed nonunion. These children were observed with loss of correction within the first 30 days after surgical treatment. This counts for a loosened soft tissue attachment. Because of displacement with periosteal injury, a loss of periosteal stability and resistance to ESIN may occur and lead to higher instability. The radial head is placed in the nail like a hat is hung on the hook. An alternative to increasing the stability could be a second nail in the radius head, as with a two-point fixation, it is no longer the hat on the hook. If intraoperative result causes one to consider instability, plate osteosynthesis should be implemented. An advantage, compared to K-wire, is to enable mobilization stable fixation. Therefore, immediate exercise is possible to avoid postoperative fixation and a better functional outcome is expected similar to elbow dislocations.

This could be seen as a preventive measure against synostosis as seen often in K-wire osteosynthesis. Transarticular

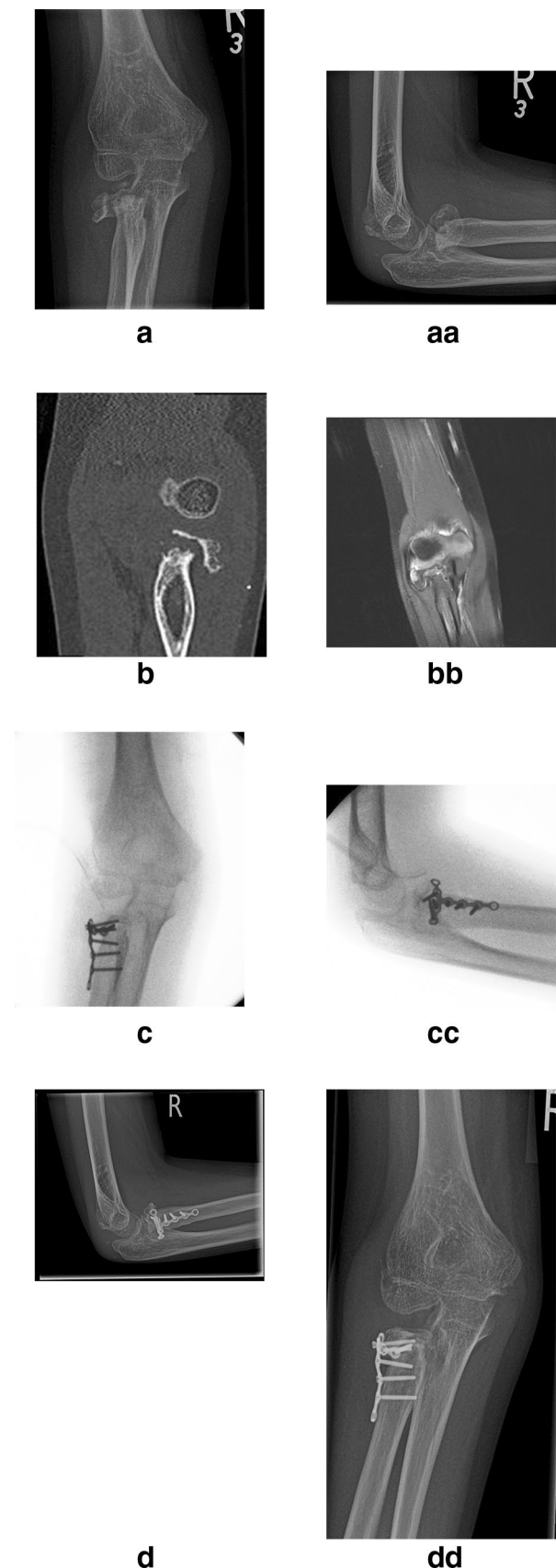




Fig. 3 (continued)

K-wire fixation we regard as critical, actually oppose this technique.

Poor results after radial neck fracture are attributed to an insufficient reposition [11]. None of our study patients presented with deficient reposition. Only in one patient, a high amount of residual instability led to renewed surgery after 2 days. 8 patients were observed with a radiologically excellent quality of reduction. We could not prove that an insufficient reduction of the radial head was responsible for the development of the pseudarthrosis.

In children under 5 years of age, the unossified radial epiphysis may not be possible to visualize in X-ray. In this case, a complete displacement of the radial head, accordingly Metaizeau type IV, can be overlooked [3]. 2 of our study patients aged 4 and 5 years presented with overlooked fractures. They were diagnosed with elbow distortion because heavy displaced fractures of the radial head were not recognized as the radial head was still mostly cartilaginous and not well visualized in radiographic diagnostics. Therefore, further imaging is indicated in young children with not yet

ossified radial head but in suspicion of elbow trauma. Ultrasound is an appropriate technique to examine the position of the radial head and of the epicondylus ulnaris humeri.

Various complaints and pain were described in cases of nonunion. Waters observed pain in three of nine children. We found 9 of 11 children suffer elbow pain. Furthermore, we noted 5 children with relevant cubitus valgus. Waters did not mention elbow valgus deformity. Results for limitation of pronation–supination of the forearm did not differ relevantly. We as well observed severe radiological deformity of the radial head like avascular necrosis, enlarged and deformed radial head, calcification, subluxation of the radial head and alteration of the proximal radioulnar joint. Changes that have not yet been described but seal the fate of the radial head are the rubbing of the radial neck and head through the metaphysis up to the breakthrough of the metaphysis through the head and usury of the capitulum and fragmentation of the head.

Preceding the perforation of the metaphysis, a defect area of the radial neck and epiphyses can be detected in variable extent. According to this phenomenon, defect zone was classified into four types. 4 children were classified type I/II representing with no defect or a defect area less than 50% of the radial head. These were found to be the young children with a completely dislocated radial head placed next to the radial neck or the ones who underwent prior intervention. All other children presented with severe substantial deformities up to fragmentation of the head. The concomitant limitations of forearm pronation–supination showed a great variety.

All three children with a dissolved and fragmented radial head showed significant elbow valgus angle compared to the healthy elbow. Existing with instability of the elbow, crepitation and reduced weight-bearing of the elbow joint. Not negligible is the axial force transmission of 60% through the radius–capitulum humeri axis. Except the three cases mentioned above and a girl (case 8), all heads were found in adhesion to the articular capsule. The movement of the metaphysis against the radial head was found to affect the head like being grounded by a mortar.

Waters has the conception that childrens with few symptoms, minor limitation of function and acceptable position of the radioulnar articulation should observe follow-up. In the Waters group [5], all children had significant limitations in turning the arm around similar to our group before the operation. After the surgical treatment of the pseudarthrosis, our group shows an improvement in movement including the prevention of further deformation of the radial head, with the exception of one child.

Metaizeau [2] considers the functional results difficult to be assessed due to posttraumatic deformation. He recommends not to intervene prior to end of growth if only minor limitations are present. As far as our experience goes, we propose to indicate a surgical treatment if nonunion is

discovered. After our experience observing a progressive deformity and destruction of the radial head up to fragmentation in many cases surgical indication is approved to obtain the head. The changes of the radial head we noticed are mostly relevant and dependent on time between fracture and presentation. The persistent changes of the radial head and neck led to continued restricted motion in the arm.

As spontaneous healing of nonunion is described in literature [3], a temporary limited observation can be considered. Inherent danger of progressive affection of the radial head and neck is present. To designate a decidedly time period of observation is difficult and not clear.

In summary, it can be said that nonunion of the radial neck remains challenging in surgical treatment.

Overall understanding of elbow injuries, elbow anatomy along with blood supply of the bone structures, are basic requirement to lead to good results in radial neck nonunion. Angle-stable osteosynthesis is a presently available facilitating technical procedure.

The sooner indication for treatment is approved, the lesser deformities of the radial neck and head may be expected. Serious concerns are raised in delaying procedure.

In spite of our very good results, it has to be pointed out, that open reduction, composition of the radial head and arthrolysis with osteosynthetic stabilization of the radial head are absolutely challenging. Concomitant complications may occur.

This surgical treatment is an elective procedure to be performed only by an experienced surgeon in elbow techniques.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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