SCIENTIFIC ARTICLE

Prognostic Factors for the Outcome of Supracondylar Humeral Fractures in Children

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Objective: To detect the influence of the type of osteosynthesis, the timing of surgery, and the experience of the surgeon on the outcome of supracondylar humeral fractures in children.

Methods: In this study we included 97 patients aged 0 to 18 years with displaced supracondylar humeral fractures that required osteosynthesis within a time period of 5 years. In detail, unstable type II as well as type III and type IV fractures were registered. Fractures were treated with Kirschner wire fixation or with elastic stable intramedullary nailing (ESIN). A C-arm was used to control the position of the fragments. Immobilization, if indicated after the operation, was achieved through the fitting of long-arm plaster, or fiberglass splints. The study was carried out retrospectively. The time period to surgery, the duration of the surgery, the type of osteosynthesis, and the experience of the surgeon were determined and correlated to the incidence of complication intraoperatively, postoperatively, and during the long-term follow-up. The hospital’s electronic archive, including all charts and radiological studies, was analyzed. Statistical significance was set at an alpha level of 0.05.

Results: Of the 97 supracondylar fractures in this study, 55 (56.7%) occurred in boys and 42 (43.3%) in girls; the average age was 5.8 years. The outcome of the operation was independent of the time interval between the trauma and the operation as well as the mode of transportation (P > 0.05) because the complication rate did not differ significantly between patients who had surgery on the same day and between patients who waited for up to 2 days for surgery. Furthermore, the duration of surgery and the experience of the performing surgeon did not influence the occurrence of any complications. However, the complication rate increased after operations performed during the night shift. During the shift between 10 pm and 2 am, the incidence of paresthesia was significantly increased (P = 0.01) compared to the shift from 7:30 am to 4:30 pm. However, no difference was detected between business and non-business days regarding any complications. In addition, ESIN and closed reductions resulted in lower complication rates than Kirschner wire fixation and open reductions in this study population.

Conclusion: In our study population, patients undergoing surgery during the night shift, Kirschner wire fixation and open reduction were associated with an increased rate of complications in comparison to operations during the day, closed reduction, and ESIN. Notably, the timing of surgery and the experience of the surgeon did not have any impact on the outcome after supracondylar humeral fracture.

Key words: Complication; Children; Elastic stable intramedullary nail; Kirschner wire fixation; Supracondylar humeral fractures

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Supracondylar humeral fractures in children

Introduction
Supracondylar humeral fractures are the most common elbow fractures in children. Boys are affected more often than girls and the average age at which these fractures occur is 6 years. The majority of supracondylar humeral fractures are extension-type injuries due to a fall onto the outstretched hand while the elbow is extended. Complications after supracondylar humeral fractures include neurovascular lesions, decreased range of motion, malalignment, and nonunion. Although this is a common fracture, controversy exists regarding whether it causes a fracture site and the ulnar nerve. However, to date, only a limited number of papers are available that report on the clinical application of ESIN in supracondylar humeral fractures.

Methods of Treatment
Fractures were treated with Kirschner wire fixation or with ESIN (as previously described by Lacher et al.). While Kirschner wires are applied at the site of the fracture and have the risk of injuring the ulnar nerve, ESIN are inserted from the proximal humerus. In 1 case, Kirschner wire and screw fixation were combined separately based on the individual decision of the attending surgeon. A C-arm was used to control the position of the fragments. Immobilization, if indicated after the operation, was achieved by the fitting of long-arm plaster, or fiberglass splints.

Patients
The study was carried out retrospectively. Patients aged 0–18 years with supracondylar fractures that required osteosynthesis with epiphysial plates who had surgery at our institution during a time period of 5 years were selected from the hospital’s electronic radiologic archive. Fractures were classified according to the AO Pediatric Comprehensive Classification. Analysis was performed using the hospital’s electronic archive including all charts, radiological studies, and laboratory studies.

Assessment of Outcomes
The following data of the patients were assessed: age, sex, time of trauma, type of fracture, concomitant injuries, vascular and sensomotory status, time of admission to the hospital, mode of transportation and treatment before admission, details of the operation and the hardware removal, medications, complications, and findings from radiological measures and from examinations.

Complications were grouped into three categories: intraoperative complications, complications occurring post-operatively before discharge, and complications that lasted until the last follow-up examination. Complications were recorded in the patient records during the hospital stay and at the follow-up examinations and reviewed within the course of this study. They included impaired range of motion, misalignment, skin perforation, paresthesia, and wound infection. The perfusion and the sensomotory status have been analyzed separately.
The time period to surgery, the duration of the surgery, the type of osteosynthesis, and experience of the surgeon were determined and correlated to the incidence of complication intraoperatively, postoperatively, and during the long-term follow up. Furthermore, it was assessed whether a change in the treatment method (Kirschner wire vs ESIN, closed reduction vs open reduction) was necessary.

Statistics
Pearson’s χ² test was applied. Statistical analysis was performed using IBM SPSS Statistics 20.0, USA. In cases of n < 5 the Fisher exact test was applied. For comparison of more than two groups, ANOVA was applied. Statistical significance was set at an alpha level of 0.05. All data were irreversibly anonymized.

Results

Study Population
The study included 97 patients with supracondylar humeral fractures. Of these, 55 (56.7%) occurred in boys and 42 (43.3%) in girls; the average age was 5.8 years. A majority of supracondylar fractures (54.8%) resulted from playing or sports and 36.1% from falls.

Timing of Surgery

Time Period to Trauma
First, the time interval from trauma to surgery was analyzed and a correlation with the mode of transportation was found. Hence, patients who walked into the emergency room (73.2%) waited longer for surgery than patients who were transported by ambulance or helicopter (26.8%). Most patients had surgery on the same day (56.7%) or on the next day (29.9%, Fig. 1A). Remarkably, the outcome regarding the complication rate and long-term impairment of motion was independent of the time interval between trauma and surgery as well as the mode of transportation (P > 0.05). This means that patients who were treated on the same day of the trauma did not show better results than patients who were operated on the following days. Furthermore, no tendency towards better results was seen regarding transportation with a helicopter, ambulance or a private car, or even public transportation.

Time of Day of Operation
Investigations into whether the time of day that the operations were performed affects the outcome revealed that most operations were completed during the day or in the evening and none between 2 am and 7:30 am (Table 1). Notably, during the shift between 10 pm and 2 am complication rates were significantly increased (P = 0.01), with a rate of 33.3% (3 out of 9 cases), whereas 6 cases of sensomotor functional deficits were counted in 52 patients (11.5%) during shift 1 from 7:30 am to 4:30 pm. However, no significant difference was seen regarding any other complications. Furthermore, 71.1% of the operations were conducted on working days and not on nonbusiness days. No difference in any complications was detected between business and non-business days (P > 0.005). Complications were assessed during the hospital stay and at follow-up examinations and included intraoperative and perioperative as well as long-term complications.

Duration of Surgery
The mean duration of surgery was 81 min, whereas the mode of duration values was captured as 50 min. Furthermore, the fastest operation took 20 min and the longest operation took 330 min. There were 6 cases that took longer than 180 min; all of these needed conversion from closed to open reduction (Table 1). Complications arising postoperatively on the ward and after discharge were not registered more often after long operations than after procedures that took less than 90 min.

Impact of Type of Osteosynthesis on the Outcome
The type of osteosynthesis was found to be influenced by the type of reduction where ESIN mainly was applied after closed reduction and Kirschner wires mostly after open reduction. In this study, we included 28 type II fractures; 24 of these were fixed with ESIN while the rest were treated with Kirschner wire osteosynthesis. Furthermore, we present 26 cases of ESIN for the more complicated type III and IV fractures. These were compared to 43 type III and IV fractures treated with Kirschner wire fixation and complication rates were lower after ESIN. It was found that 78.5% of type IV fractures were treated with Kirschner wires (51.3% after open reduction and 27.2% after closed reduction). However, ESIN after closed reduction was possible in 20.5% of type IV fractures and ESIN after open reduction was applied in 1 case (Fig. 2). Remarkably, complications during the hospital stay (Table 2) were more frequent after Kirschner wire fixation (P = 0.027). In the follow-up examination, the most frequent complication was the occurrence of an impaired range of motion in 46% after ESIN and 38% after Kirschner wire fixation. Nevertheless, after Kirschner wire fixation additional complications (misalignment [4%], skin perforation of the Kirschner wires [8.9%], wound infection [6%] and 3 patients with paraesthesia) were diagnosed during follow-up visits (Fig. 3A).

Impact of the Type of Reduction on the Outcome
Furthermore, complication rates after open and closed reduction were compared analyzing 66 closed and 31 open reductions. It was revealed that of the more complex type III and IV fractures (n = 69), 39 cases could be reduced in a closed manner and, notably, of those, 25 fractures were treated with ESIN and 14 with Kirschner wire fixation. Interestingly, no correlation was found between the method of open reduction and the incidence of postoperative complications during the hospital stay (P = 0.3). However, in the follow-up examination, the rate of misalignment and delayed consolidation according to the X-ray, as well as skin perforation by Kirschner wires and wound infections, was increased.
after open reduction, with 29% in comparison to 9% after closed reduction ($P = 0.002$) (Fig. 3B). Nevertheless, the incidence of paresthesia was assessed by clinical examination and nerve conduction velocity testing during the follow-up visits and was higher after closed reduction. In detail, after open reduction, no patient showed any sensomotory deficit during the follow-up visit, whereas 3 patients who had undergone closed reduction revealed a sensory deficit.

**Experience of the Surgeon**
In order to compose training programs for surgeons, the qualification of the surgeon who performed the osteosynthesis was assessed. For every procedure, a consultant or attending physician was present. However, most operations were undertaken by experienced residents (40.2%) or consultants themselves (36.1%, Table 3). Here, the rate of complications that were detected after supracondylar humeral fracture was independent of the experience of the surgeon ($P > 0.05$).

**Discussion**
This study analyses parameters potentially influencing the outcome after osteosynthesis of supracondylar humerus fractures in children. Our data clearly suggest that Kirschner wire osteosynthesis, in comparison to ESIN, and open reduction as well as timing of surgery during the night shift between 10pm and 2am result in an increase of postoperative complications. However, the time interval to surgery following the fracture, as well as trauma mechanism, mode of transportation, duration of surgery, and experience of the operating surgeon in the presence of a consultant pediatric surgeon do not influence the occurrence of complications.

The major choice at the beginning of surgery is the mode of osteosynthesis. The comparison of Kirschner wire fixation to ESIN revealed a significantly lower complication rate after ESIN. While, according to the literature, SCHF type III and IV are mainly fixated with Kirschner wires, $^{25}$

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**Table 1: Time of day that surgery was performed**

| Shift  | Time               | Number of operations | Percentage of all operations |
|--------|--------------------|----------------------|------------------------------|
| Shift 1| 7:30am–4:40pm      | 52                   | 53.6                         |
| Shift 2| 4:31pm–10:00pm     | 36                   | 37.1                         |
| Shift 3| 10:01pm–2:00am     | 9                    | 9.3                          |
| Shift 4| 2:01am–7:29pm      | 0                    | 0                            |
| All    | —                  | 97                   | 100                          |

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*Fig. 1* Analysis of the timing of the procedure. (A) The time from trauma to surgery and reveals that the majority of patients was operated on on the day of the trauma or 1 day after. (B) Demonstrates that most procedures took 1 hour.
the treatment of unstable type II supracondylar fractures has been a subject of controversy because simple immobilization or cuff and collar are as well accepted as closed reduction and Kirschner wire fixation. However, the method of closed reduction and ESIN has been reported to have good results in type II fractures as well. In this study, we included 28 SCHF type II fractures; 24 of these were fixated with ESIN, while the rest were treated with Kirschner wire osteosynthesis.

Elastic stable intramedullary nailing is usually not applied for more complex fractures, including type III and IV fractures, and Kirschner wire fixation is still regarded as the standard procedure. However, we present 26 cases of ESIN for these more complicated fractures. These were compared to 43 type III and IV fractures treated with Kirschner wire fixation and better results were revealed than for Kirschner wire fixation. However, in our study we found that not only does open reduction increase the risk of complications after surgery in comparison to closed reduction, but the mode of osteosynthesis was also shown to change the rate of complications because we found a higher incidence of complications after Kirschner wire fixation. An advantage of ESIN is that the cast-free treatment after surgery as opposed to cast treatment for 4 weeks after Kirschner wire fixation leads to early mobilization and less impairment during everyday activities. Furthermore, the necessity of exact anatomic reduction to place the nails into the distal humerus allows for no more than 10° of rotational malalignment as well as avoiding the development of cubitus varus and valgus. Another advantage is the protection of the ulnar nerve by introduction of the ESIN at the proximal humerus as opposed to a risk of 3%-4% for ulnar nerve lesions with the use of Kirschner wires. These benefits seem to rule out the drawbacks that are being discussed, including the need of two surgeons for this procedure or possibly prolonged operations. Interestingly, the main postoperative complication that occurred after ESIN in our study is an impaired range of motion. However, there is a similar rate of impaired range of motion after Kirschner wire fixation, so that this finding in combination with the lower rate of infection and pin perforation as well as the abovementioned advantages with good functional results lead to our recommendation of using ESIN for the treatment of supracondylar humerus fractures in children, and especially for type III and IV supracondylar fractures.

Another major factor under discussion is timing of surgery. Because nerve lesions and vascular lesions must
inevitably be treated immediately, these cases were excluded from this study. Analysis of the time period between trauma and surgery revealed no increased rate of complications when surgery was postponed. Although this study only differentiated the day of trauma and the number of days after trauma as opposed to recording the hours after trauma as done in other studies, our data provide evidence that surgery on the day of trauma does not enhance the outcome of surgery. However, although there are reports that are in agreement with this finding, our results are in contrast with several other studies that have reported more complications after operations that have been postponed.

Fig. 3 (A) Complications during follow up were considered and a lower rate was noted after elastic stable intramedullary nail (ESIN) than after Kirschner wire fixation. Two cases of a combined osteosynthesis with ESIN/Kirschner wire and screw/Kirschner wire were excluded in this analysis. (B) Comparison of closed to open reduction demonstrated a higher complication rate after open reduction.
Nevertheless, after analyzing a large study population here and in agreement with the latest studies addressing this question, we conclude that the operation should be postponed to avoid the night shift. Furthermore, although previous studies by Goldstein and Bell and Redelmaier have discussed the “weekend effect,” with an increased rate of complications after surgery on the weekend, this study cannot confirm their findings because complications were not detected more often when operations were performed on the weekend.

In the literature, controversy also exists regarding the experience of the surgeon. Some previous reports have stated that experience improves the outcome because 75% of problems after surgery are related to the surgeon, while others deny that the experience influences the occurrence of long-term complications. In this study, we could not detect any difference between the outcome of fractures that were operated on by an experienced surgeon or a resident. However, if a resident was performing the surgery, there was always a consultant assisting. This is in agreement with the recommendation of a previous study and is especially relevant for the training program of surgeons because this study emphasizes that letting a young surgeon perform the osteosynthesis of any supracondylar humeral fracture in the presence of a consultant will not increase the risk of complications and can, therefore, be included in the training program. Because skills must be acquired by the residents during their training, this is a very important finding.

The limiting factors of this study are its retrospective design that also made it impossible to introduce classifications of symptoms that we assessed (e.g. the degree of pain). Furthermore, the observation period was quite short and we need to perform a follow-up study to evaluate the long-term outcomes of the operations.

In conclusion, we found that the outcome after supracondylar humeral fracture in children was better after closed reduction and ESIN than after Kirschner wire fixation and open reduction in our study population. Notably, the complication rate was significantly lower after operations that were carried out during the day shift and not in the late night shift. In this study, the trauma mechanism, the mode of transportation, the time interval to surgery, as well as the duration of the procedure did not influence the outcome, and the operation could be performed safely by a resident.

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**References**

1. Omid R, Choi PD, Skaggs DL. Supracondylar humeral fractures in children. J Bone Joint Surg Am, 2008, 90: 1121–1132.
2. Mangwani J, Nadarajah P, Paterson JM. Supracondylar humeral fractures in children: ten years’ experience in a teaching hospital. J Bone Joint Surg Br, 2006, 88: 362–365.
3. Singer G, Kraus T, Ruttenstock EM, Ferlic P, Eberl R. Antegrade nailing can prevent cubitus varus and valgus after pediatric supracondylar fractures with impacted columns. J Orthop Trauma, 2013, 27: e285–e290.
4. Woratanarat P, Angsanuntsuk C, Rattanasiri S, Attia J, Woratanarat T, Thakkinstant A. Meta-analysis of pinning in supracondylar fracture of the humerus in children. J Orthop Trauma, 2012, 26: 48–53.
5. Cheng JC, Lam TP, Maffulli N. Epidemiological features of supracondylar fractures of the humerus in Chinese children. J Pediatr Orthop B, 2001, 10: 63–67.
6. Barr LV. Paediatric supracondylar humeral fractures: epidemiology, mechanisms and incidence during school holidays. J Child Orthop, 2014, 8: 167–170.
7. Khosbin A, Leroux T, Wasserstein D, et al. The epidemiology of paediatric supracondylar fracture fixation: a population-based study. Injury, 2014, 45: 701–708.
8. BabalJC, Mehman CT, Klein G. Nerve injuries associated with pediatric supracondylar humeral fractures: a meta-analysis. J Pediatr Orthop, 2010, 30: 263–263.
9. Ramachandran M, Birch R, Eastwood DM. Clinical outcome of nerve injuries associated with supracondylar fractures of the humerus in children: the experience of a specialist referral centre. J Bone Joint Surg Br, 2006, 88: 90–94.
10. Eberl R, Eder C, Smolle E, Weinberg AM, Hoellwarth ME, Singer G. Iatrogenic ulnar nerve injury after pin fixation and after antegrade nailing of supracondylar humeral fractures in children. Acta Orthop, 2011, 82: 606–609.
11. Joiner ER, Skaggs DL, Arkader A, et al. Iatrogenic nerve injuries in the treatment of supracondylar humerus fractures: are we really just missing nerve injuries on preoperative examination? J Pediatr Orthop, 2014, 34: 388–392.
12. Griffin KU, Walsh SR, Markar S, Tang TY, Boyle JR, Hayes PD. The pink pulseless hand: a review of the literature regarding management of vascular complications of supracondylar humeral fractures in children. Eur J Vasc Endovasc Surg, 2008, 36: 697–702.
13. Storm SW, Williams DP, Khoury J, Lubahn JD. Elbow deformities after fracture. Hand Clin, 2006, 22: 121–129.
14. Wang YL, Chang WN, Hsu CJ, Sun SF, Wang JL, Wong CY. The recovery of elbow range of motion after treatment of supracondylar and lateral condylar fractures of the distal humerus in children. J Orthop Trauma, 2009, 23: 120–125.
15. Mulpuri K, Wilkins K. The treatment of displaced supracondylar humerus fractures: evidence-based guideline. J Pediatr Orthop. 2012, 32: S143–S152.
16. Davis RT, Gorczyca JT, Pugh K. Supracondylar humerus fractures in children. Comparison of operative treatment methods. Clin Orthop Relat Res, 2000, 376: 49–55.
17. Lacher M, Schaeffer K, Boehm R, Dietz HG. The treatment of supracondylar humeral fractures with elastic intramedullary nailing (ESIN) in children. J Pediatr Orthop. 2011, 31: 33–38.
18. Schaffer K, Bohn R, Dietz HG. Elastic stable intramedullary nailing (ESIN) of supracondylar fractures of the humerus in children. Unfallchirurg, 2007, 110: 852–858.
19. Prevot J, Lascombes P, Metaizeau JP, Blanquart D. Supracondylar fractures of the humerus in children: treatment by downward nailing. Rev Chir Orthop Reparatrice Appar Mot, 1996, 76: 191–197.
20. Lehner M, Schuster B, Dietz HG. Strategies in the treatment of supracondylar fractures of the humerus in children - proven and controversial. Zentralbl Chir, 2014, 139: 613–620.
21. Llopu CL, Simillis C, Hutchinson JR. A systematic review of early versus delayed treatment for type III supracondylar humeral fractures in children. Injury, 2009, 40: 245–248.
22. Kronner JM Jr, Legakis JE, Kovacevic N, Thomas RL, Reynolds RA, Jones ET. An evaluation of supracondylar humerus fractures: is there a correlation between postponing treatment and the need for open surgical intervention? J Child Orthop, 2013, 7: 131–137.
23. Mayne AI, Perry DC, Bruce CE. Delayed surgery in displaced paediatric supracondylar fractures: a safe approach? Results from a large UK tertiary paediatric trauma centre. Eur J Orthop Surg Traumatol, 2014, 24: 1107–1110.
24. Slongo T, Audige L, Schlickewei W, Clavert JM, Hunter J, International Association for Pediatric T. Development and validation of the AO pediatric comprehensive classification of long bone fractures by the pediatric expert group of the AO Foundation in collaboration with AO clinical investigation and documentation and the international association for pediatric traumatology. J Pediatr Orthop, 2006, 26: 43–49.
25. Kim WY, Chandru R, Bonshahi A, Paton RW. Displaced supracondylar humeral fractures in children: results of a national survey of paediatric orthopaedic consultants. Injury, 2003, 34: 274–277.
26. Kennedy JG, El Abed K, Soffe K, et al. Evaluation of the role of pin fixation versus collar and cuff immobilisation in supracondylar fractures of the humerus in children. Injury, 2000, 31: 163–167.
27. Leet AI, Frisancho J, Ebramzadeh E. Delayed treatment of type 3 supracondylar humerus fractures in children. J Pediatr Orthop, 2002, 22: 203–207.
28. Han QL, Wang YH, Liu F. Comparison of complications and results of early versus delayed surgery for Gartland type III supracondylar humeral fractures in pediatric patients. Orthop Surg, 2011, 3: 242–246.
29. Abbott MD, Buchler L, Loder RT, Calcutt CE. Gartland type III supracondylar humerus fractures: outcome and complications as related to operative timing and pin configuration. J Child Orthop, 2014, 8: 473–477.
30. Buturovic S, Krupic F. Comparison of treatment results for fractures of the distal humerus in children according to the indication for conservative or surgical solution. Mater Sociomed, 2014, 26: 242–245.
31. Yildirim AO, Unal VS, Oken OF, Gulcek M, Ozsular M, Ucaner A. Timing of surgical treatment for type III supracondylar humerus fractures in pediatric patients. J Child Orthop, 2009, 3: 265–269.
32. Goldstein SD, Papandria DJ, Aboagye J, et al. The “weekend effect” in pediatric surgery - increased mortality for children undergoing urgent surgery during the weekend. J Pediatr Surg, 2014, 49: 1087–1091.
33. Bell CM, Redelmeier DA. Mortality among patients admitted to hospitals on weekends as compared with weekdays. N Engl J Med, 2001, 345: 663–668.
34. Padman M, Warwick AM, Fernandes JA, Flowers MJ, Davies AG, Bell MJ. Closed reduction and stabilization of supracondylar fractures of the humerus in children: the crucial factor of surgical experience. J Pediatr Orthop B, 2010, 19: 298–303.
35. Slongo TF. The choice of treatment according to the type and location of the fracture and the age of the child. Injury, 2005, 36: A12–A19.
36. Dodds SD, Grey MA, Bohi DD, Mahoney EM, DeLuca PA. Clinical and radiographic outcomes of supracondylar humerus fractures treated surgically by pediatric and non-pediatric orthopedic surgeons. J Child Orthop, 2015, 9: 45–53.
37. Farley FA, Patel P, Craig CL, et al. Pediatric supracondylar humerus fractures: treatment by type of orthopedic surgeon. J Child Orthop, 2008, 2: 91–95.
38. Liu RW, Roocroft J, Bastrum T, Yasay B. Surgeon learning curve for pediatric supracondylar humerus fractures. J Pediatr Orthop, 2011, 31: 818–824.
39. Reznick RK, MacRae H. Teaching surgical skills–changes in the wind. N Engl J Med, 2006, 355: 2664–2669.