Acute Infections After Fracture Repair

Management With Hardware in Place

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Abstract Managing infections in fractures treated with open reduction and internal fixation is an ongoing dilemma. Little published data exist to support the current practice of treating these infections with retained hardware, irrigation, débridement, and antibiotic suppression. We evaluated the effectiveness of this approach. We identified potential subjects from a central trauma database and selected them based on chart review and specific inclusion and exclusion criteria. We divided the patients into two groups. Patients achieving successful union with original hardware in place were considered as having successful results and patients who required hardware removal before healing were considered to have failed results. Data, including age, gender, tobacco use, diabetic status, site of fracture, Orthopaedic Trauma Association class, open grade, type of fixation, joint involvement, and organism, were gathered and

compared between the groups by analysis of variance. Sixty-nine cases were available for analysis. Forty-seven (68%) were successful and 22 (32%) were unsuccessful. Average time to healing was 130 days. Most of the failures occurred within 120 days from the time of injury. Smoking was a major risk factor with a 3.7 times greater likelihood of procedures being unsuccessful per month than procedures among nonsmokers. Treating infected fractures with hardware in place is less successful than widely believed. **Level of Evidence:** Level IV, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

Introduction

Management of infections that arise in the early postoperative period after treatment of a fracture with open reduction and internal fixation (ORIF) is an ongoing dilemma. It is widely accepted that deep infections cannot be cured in the presence of hardware [3, 18]. However, removing hardware in the presence of an unhealed fracture greatly complicates management of the infection and the fracture. Standard orthopaedic dogma suggests the fractures will heal in the presence of infections as long as the hardware remains stable [2, 4, 6, 20, 21]. Thus, the standard treatment for an acute deep infection after ORIF is to reduce the bacterial load with irrigation and débridement and then to suppress the infection until the fracture heals [9, 20]. Some authors suggest the infection often will resolve once the fracture has healed [11, 14]. Although this view is widely held, there is little published evidence evaluating its accuracy. This approach has been more or less standard at our institution for several years. The primary purpose of this study was to determine the success

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Each author certifies that his or her institution has approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent was obtained.

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rates for achieving union and resolving infection using this strategy. We also aimed to identify patient and fracture characteristics that might have contributed to the strategy's success or failure.

Materials and Methods

An initial cohort of patients was identified by searching the combined Orthopaedic Trauma Registry of the Brigham and Women's Hospital and the Massachusetts General Hospital (Orthopedic Data Utility for Documentation and Education). The registry includes all surgical procedures by Current Procedural Terminology code as entered by the attending surgeon and the Orthopaedic Trauma Association (OTA) Fracture Classification and Gustilo-Anderson Open Fracture Classification as entered by the resident and checked by the attending physician at the time of the first surgical procedure (MSV, RMS, MBH, TB, DL, DR) [5, 12]. We searched the database for patients who were returned to the operating room for irrigation and débridement within 16 weeks of their definitive fracture surgery. The inpatient and outpatient charts of patients identified by this search then were reviewed to identify patients who were returned to surgery for an acute infection.

To be included, patients must have had definitive operative fracture management within 3 weeks of injury and had an acute infection develop between 1 and 16 weeks after definitive fixation and before union. We defined infection as the appearance of an erythematous draining wound that required débridement or persisted for more than 3 weeks. We excluded fractures treated definitively with external fixators. There were 18 patients who had hardware removed at the initial débridement because the fixation was unsuccessful. We did not include these patients in this study. To be included, open fractures required definitive fixation and appropriate soft tissue coverage within 4 weeks and before the onset of infection. The date of definitive fixation was considered to be the time when internal fixation was placed. For fractures that had temporary fixators, definitive fixation occurred when the external fixator was exchanged for internal fixation. We identified 83 consecutive patients, aged 18 to 87 years, with 84 cases of acute infection after ORIF from July 1998 until January 2005. One patient was lost to followup before union and two had less than 6 months followup with hardware still in place and were excluded. One patient died 3 weeks after definitive fixation. One patient was believed to have a stitch abscess without evidence of deep wound infection and was excluded to avoid confusion. This left 78 patients with 79 cases for analysis. Of the 79 cases, 69 had suppressive treatment (plus or minus débridement as necessary), and 10 had hardware revision at the initial débridement.

Table 1. Distribution of all cases by OTA class

OTA class	OTA A	OTA B	OTA C	Total
Number of fractures	22	27	30	79

OTA = Orthopaedic Trauma Association.

There were 56 closed and 23 open fractures (two Grade I, eight Grade II, five Grade IIIA, and eight Grade IIIB open fractures). There were 22 simple (A type), 27 intermediate (B type), and 30 complex (C type) fractures according to the OTA classification (Table 1). All fractures had definitive ORIF within 24 days of initial injury (average, 4.1 days). There were 31 (40%) patients who smoked and 15 (19%) who had diabetes. Nineteen patients required soft tissue coverage and 50 cases involved a joint. Fifty-two of the patients had surgical débridement when the infection was diagnosed, and 17 initially were treated with intravenous antibiotics alone. Methicillin-resistant *Staphylococcus aureus* was identified in 56% of the cases in which culture results were available (Table 2).

We recorded dates of onset, duration of antibiotics, and time before initial débridement or hardware removal. Culture data from intraoperative deep tissue samples taken at the time of initial débridement were recorded. If no initial débridement was performed (for example, in cases of infection treated with antibiotics alone), then we assumed there was infection in the presence of a persistent draining wound for at least 3 weeks as documented in the clinic notes.

Followup radiographs were taken at the time of regular clinic visits and were reviewed by the author (ER) and by attending surgeons (MSV, RMS, MBH, TB, DL, DR). All radiologic studies and clinical examinations were performed at the Brigham's and Women's Hospital or Massachusetts General Hospital with the exception of four

Table 2. Distribution of cases by organism present in culture

Culture result	Number of cases
No growth	3
Methicillin-resistant <i>Staphylococcus aureus</i>	48
Methicillin-susceptible <i>Staphylococcus aureus</i>	14
<i>Escherichia coli</i>	2
Enterococci species	4
<i>Pseudomonas aeruginosa</i>	2
<i>Morganella morganii</i>	1
<i>Proteus mirabilis</i>	1
<i>Klebsiella</i>	2
<i>Citrobacter</i> species	1
Streptococci species	1
Enterobacter species	4
<i>Serratia</i> species	2

patients who received part of their treatment at outside hospitals and had adequate documentation of history on presentation. We considered a fracture united when plain radiographs or computed tomography scan showed bridging bone across the fracture and the patient could bear full weight without pain.

We defined success as achieving fracture union with the original hardware in place whether or not infection persisted. A minimum of 6 months followup was required for all patients who achieved union. Fractures initially treated with hardware in place that later required hardware revision to achieve union were considered failures and were included even if followup was less than 6 months. We considered patients initially managed with single-stage hardware exchange at the initial débridement a special group. The hardware (intramedullary rods or plates) was exchanged and the medullary canals were reamed and wound beds débrided.

Patients selected had their information entered into standard Microsoft Excel spreadsheets (Microsoft, Redmond, WA). Each patient had data entries for age, gender, date of injury, site and OTA fracture classification, type of fracture fixation, date of definitive ORIF, date of soft tissue coverage, date of infection onset, date of initial débridement, number of débridements, date of infection resolution, date of fracture union, duration of antibiotics, and date(s) of reinfection. Specific patient comorbidities, including diabetes, tobacco use, and presence of open fracture, also were included.

We performed univariate analysis to assess differences in patient and surgical characteristics between failures and nonfailures with Fisher's exact test or chi square test for categorical variables and the Mann-Whitney U test for continuous variables that were not normally distributed (duration of antibiotic use, number of irrigations and débridements). This analysis was applied to the patients who had suppressive therapy but not in the group of patients who had acute exchange of the original hardware. Age was compared using the two-sample Student's t-test. We used the Kaplan-Meier product limit method to estimate survivorship with 95% confidence limits around the curves determined by Greenwood's formula and subgroups compared by the log rank test [7]. The multivariate Cox regression model was applied to identify independent predictors of failure with the likelihood ratio test as the measure of significance. The Cox proportional hazards regression analysis adjusted for possible confounding among several different covariates, including age, gender, fixation, OTA class, site of fracture, smoking status, diabetes, type of microorganism, joint involvement, open fracture, duration of antibiotics, and number of irrigations and débridements, using a stepwise backward selection procedure [16]. The proportional hazards analysis assumes

that as the hazards change, the distance between the two curves stays about the same and this proportionality assumption of the model was assessed graphically using a log-minus-log plot to confirm that the two curves were essentially equidistant. The hazard ratio and 95% confidence interval were calculated for multivariate risk factors of failure because the interpretation of the hazard ratio makes sense only for noteworthy predictors of outcome. Analysis of the data was performed using SPSS 14.0 for Windows (SPSS Inc, Chicago, IL). For all statistical comparisons, a two-tailed value of $p < 0.05$ was considered statistically significant.

Results

This treatment was considered successful in 47 (68%) of the 69 patients. The treatment failed in 22 (32%) of the 69 patients. One of the 22 patients who had failures was lost to followup. Two of the 22 had hip resections and one had a hemiarthroplasty. All three of these patients remained uninfected at the end of the study. Thirteen of the 22 patients who had failures achieved successful union with additional treatment interventions, although the infection remained in one patient 1 month after successful union. The five remaining patients had persistent nonunion. Of these five, infection remained in two patients and three show no signs of infection.

The average time to healing in the successful group was 130 days. The average number of irrigations and débridements was 2.1. Cases that were judged unsuccessful were those in which the hardware had failed or those in which treatment other than débridement and suppressive antibiotics was instituted. Treatment after failure of initial fixation in the 22 patients who were unresponsive to suppressive therapy was delayed revision in eight patients, external fixation in three patients, bivalve casts or splints and protected weightbearing in six patients, Girdlestone procedure in two patients, bone graft without hardware in two patients, and no additional treatment in one patient.

Ten patients were treated with single-stage revision of hardware. There were four rod exchanges, three plate revisions, two primary ankle fusions, and one revision of an olecranon tension band to a plate. We performed one of the plate revisions to correct a previously malreduced fracture and two were used to treat nonunions in patients with clinically healed wounds. Cultured specimens from these three later were positive. Six patients (60%) achieved successful union with revised hardware in place. The two ankle fusions each required an additional revision before achieving union and were considered unsuccessful. Two of the four rod exchanges failed the initial exchange. One case resulted in a below-knee amputation as a result of

Table 3. Univariate analysis of patient and fracture characteristics according to outcome

Variable	Success (N = 47)	Failure (N = 22)	p Value
Age, years	51.3 ± 17.2	52.6 ± 16.3	0.77
Gender, number (%)			
Male	19 (68)	9 (32)	0.97
Female	28 (68)	13 (13)	
Fixation, number (%)			
Plates/screws	45 (68)	21 (32)	0.99
Rods	2 (67)	1 (33)	
Orthopaedic Trauma Association class, number (%)			
A	9 (47)	10 (53)	0.02*
B	13 (59)	9 (41)	
C	21 (87)	3 (13)	
Site of fracture, number (%)			
Lower extremities	41 (69)	18 (31)	0.72
Upper extremities	6 (60)	4 (40)	
Soft tissue coverage, number (%)			
Yes	11 (73)	4 (27)	0.76
No	36 (67)	18 (33)	
Smoking, number (%)			
Yes	14 (52)	13 (48)	0.03*
No	33 (79)	9 (21)	
Diabetes, number (%)			
Yes	10 (71)	4 (29)	0.98
No	37 (67)	18 (33)	
Open fracture, number (%)			
Yes	13 (68)	6 (32)	0.99
No	34 (68)	16 (32)	
Joint involvement, number (%)			
Yes	33 (75)	11 (25)	0.12
No	14 (56)	11 (44)	
Microorganism, number (%)			
Methicillin-resistant Staphylococcus aureus	27 (69)	12 (31)	0.94
Methicillin-susceptible Staphylococcus aureus	7 (70)	3 (30)	
Other	13 (65)	7 (35)	
Number of irrigations and débridements			
Median (IQR)	3 (1–4)	3 (1–4)	0.16
Range	0–8	0–11	
Duration of antibiotics, days			
Median (IQR)	42 (42–98)	55 (42–84)	0.70
Range	10–250	14–272	

* Statistically significant; IQR = interquartile range (25th to 75th percentile).

overwhelming methicillin-susceptible *Staphylococcus aureus* infection and one case was revised to a plate for persistent malunion. The time to union averaged 232 days.

The average number of irrigations and débridements was three.

Univariate analysis suggested OTA Type C was associated with successful outcomes ($p = 0.02$) (Table 3). However, the multivariate analysis (Table 4) eliminated fracture classification as an independent predictor for outcome. The univariate and multivariate analyses identified smoking as the only independent predictor of failure. The remaining factors did not predict success or failure (Table 4). The majority of the infected fractures that failed débridements and antibiotics with retained hardware failed early (before 3 months) from the time of initial surgery. The median survivorship for the study group was approximately 8 months (Fig. 1). Patients who smoked were at a significantly higher (log rank test = 6.85, $p = 0.009$) risk of experiencing failure than nonsmokers, and the curves illustrate more failures and earlier failures in the smoking group (Fig. 2). The multivariate Cox model confirmed smoking was an independent predictor of failure with patients who smoked estimated to have a risk of failure 3.7 times higher than nonsmokers (95% confidence interval, 2.0–8.1).

In a group of 47 patients who were managed successfully to union by suppressive therapy, 19 had hardware removed for persistent infection (18 patients) or because of the patient's wishes (one patient). Twenty-eight patients had hardware that remained in place after union. Of the group with retained hardware, 10 (36%) had recurrent infections develop that required hardware removal. In the group of 19 with hardware removed after union, three (16%) also had recurrent infections develop after a minimum of 33 days (range, 33–365 days) free of clinical infection.

Discussion

Sixty-eight percent of the 69 patients with infected fractures who underwent attempted treatment with hardware in place achieved successful union through irrigations and débridements and antibiotics alone. The remaining 32% required additional intervention either in the form of hardware removal or exchange of hardware before achieving successful union. This is far different than previous reports of as much as a 95% success rate when treating infected nonunions with hardware in place on which we have based current standards of treatment [11, 14]. The results are even more disappointing if success is defined as union with no infection. Eighteen of the 47 successful cases had hardware removed for persistent infection after union, and three of these had recurrent infection develop. Another 10 patients had no sign of infection at the time of union but later had an infection

Table 4. Results of multivariate Cox proportional hazards regression analysis

Variable	Likelihood ratio test	p Value	Hazard ratio	95% Confidence interval
Age	0.57	0.45		
Gender	0.23	0.63		
Fixation (rods versus plates)	0.07	0.80		
Orthopaedic Trauma Association class	3.58	0.17		
Site of fracture	0.02	0.88		
Smoking	7.90	0.005*	3.7	2.0–8.1
Diabetes	0.50	0.48		
Soft tissue coverage	0.12	0.73		
Open fracture	2.34	0.13		
Joint involvement	0.08	0.78		
Type of microorganism	0.12	0.94		
Number of irrigations and débridements	0.85	0.36		
Duration of antibiotics	1.37	0.24		

* Statistically significant multivariate predictor of failure.

Fig. 1 The figure shows the survivorship curve for patients managed with suppressive therapy.

develop that required hardware removal. Moreover, only 49% of the original study group achieved healing and was free of infection 6 months after the study period.

Analyzing variance (Table 3) revealed patients who smoked had a far greater risk of failure than nonsmokers (univariate $p = 0.03$). This was confirmed by multivariate analysis in which patients who smoked were estimated to be 3.7 times more likely to have treatment fail each month than nonsmokers (hazard ratio, 3.7; $p = 0.005$) independent of their other characteristics (Table 4). In the univariate analysis, it also appeared OTA Type C was associated with successful outcome ($p = 0.02$). However, by multivariate analysis, OTA class did not show a major association. The remaining factors, including age, gender, type of fixation, anatomic site of fracture, diabetes, type of organism, presence of open fracture, or joint involvement, did not appear to have a greater predisposition toward failure or

Fig. 2 The figure shows the survivorship curves for patients who smoked and those who did not smoke.

success. In addition, there did not appear to be any considerable difference in the number of débridements or duration of antibiotic treatment between the cases with successful or failed treatment.

In the survivorship analysis (Fig. 1), we noted the majority of the infected fractures that failed débridements and antibiotics with retained hardware failed early (before 3 months) from the time of initial surgery. The median survivorship for the study group was approximately 8 months. Examining the effects of smoking more closely with a second Kaplan-Meier curve (Fig. 2), we noted patients who smoked had less than a 50% rate of survivorship at 12 months and also tended to experience failed treatment earlier compared with nonsmokers who fared much better.

We also observed 36% of the patients with successful results who had hardware left in place after union had

reinfection develop compared with 16% of those who had hardware removed at the time of union. We suspect the true recurrence rate after union of an infected fracture is much higher. It is well known that osteomyelitis can recur many years after the initial infection [4]. Postunion followup of our patients was relatively short. It is possible more patients with or without hardware in place will have an infection develop in the future. However, our data suggest patients with hardware left in place are at a higher risk than those who have had their hardware removed.

This study had several limitations. Defining what constitutes infection is always difficult and is particularly difficult in a retrospective study. Lacking a better definition, we chose to accept return to surgery for irrigation and débridement or wound drainage greater than 3 weeks as indicative of infection. We believed these criteria most accurately reflected clinical practice because cultures taken in the operating room can be negative even in the face of obvious infection, and contamination from skin flora makes cultures taken in the clinic difficult to interpret. Moreover, some of the cases we studied may not have been infected. However, assuming these cases would have been more likely to heal without complication, removing them would have further lowered our success rate. Similarly, our criteria for union were not stringent. Neither the radiographs nor the patients were evaluated using set criteria for union. We depended on the surgeons' evaluations as indicated in their clinic notes. We may have called cases healed that were not and removing them would again have lowered our success rate. Therefore, this study has many limitations common to retrospective studies. It is a retrospective examination and has no matched pair or cohort population for comparison. It lacks a cohort group for comparison as well as stringent outcome assessment and functional outcome assessment. It identifies differences in a subset of trauma patients who had acute infections when compared with differences cited in previously published data; however, further study is needed to determine the exact etiology of these differences. Most important, the patients were not managed by any true protocol. Nevertheless, the patients were managed according to the standard dogma: leave stable hardware in place until the fracture heals.

Our study suggests it is possible to achieve union and manage infection with hardware in place. However, the success rate (69%) is not as high as one would like. In addition, the infection recurrence rate after union remains high whether or not the hardware has been removed indicating the infection was not cured even with hardware removal. This suggests alternate protocols should be considered. One possibility would be to consider acute hardware exchange at the time of acute infection. We had too few cases in this group to draw any conclusion. However, our findings suggest the approach is not

promising. Two of the four patients who had rod exchanges did not achieve healing and one had persistent infection. Two of the patients had revision surgery to ankle fusion and both required additional surgeries to achieve arthrodesis. The three plate exchanges initially were not recognized as having infection, and only had infection diagnosed by deep culture at the time of surgery. Thus, only the patient who had an olecranon tension band converted to a plate could truly be considered as having a successful result.

Another strategy would be to consider removal of hardware with débridement followed by staged, delayed treatment of the fracture. The standard treatment for an infected total joint is to remove the joint, deliver high concentrations of local antibiotics, and to reimplant the joint once the infection has been cleared. Success rates for treating total joint infections with the prosthesis in place are disappointingly low, ranging from 15% to 54% [1, 10, 13, 15, 19]. On the other hand, success rates for débridement followed by delayed reconstruction have been reported at 94% and 100% [8, 17]. This is considerably more attractive than our 69% success rate. Thirteen of the 22 patients who did not respond to suppressive treatment went on to heal once suppressive treatment was abandoned and the infected nonunion was managed as a case of chronic osteomyelitis, and only one patient had persistent infection using this method.

Trauma surgeons have avoided staged protocols as a result of the difficulty in managing infected nonunions without stabilizing hardware in place. This is certainly a consideration for articular fractures. However, for nonarticular fractures, it may be worth considering temporarily stabilizing the fracture either with a cast or an external fixator while the infection is cleared. This may be particularly true for patients who smoke. The success rate for suppressive therapy in patients who smoke was only 52%.

In cases in which it is necessary to leave hardware in place, it may be worth considering prolonged combination therapy. We have typically treated acute infections with 6 weeks of bacteria-specific intravenous antibiotics. There is some evidence that prolonged combination therapy is more effective. Zimmerli et al. studied the management of infections with hip or knee prostheses or osteosynthesis hardware left in place [22]. Twenty-four patients with *Staphylococcus aureus* or coagulase-negative *Staphylococci* were randomized to two groups. Methicillin-resistant cases were included. The patients were treated with 2 weeks of flucoxacillin or vancomycin plus either rifampin or placebo. After 2 weeks, the flucoxacillin or vancomycin was replaced with ciprofloxacin, but one group continued rifampin, whereas the other continued placebo. Treatment was continued for 3 months for patients with hip prostheses and osteosynthesis hardware and 6 months for patients with

knee prostheses. The group that continued ciprofloxacin and rifampin had a 100% cure rate, whereas the cure rate for the placebo group was only 58%.

It is possible to achieve union of a fracture with hardware in place. However, the success rate is low and the infection recurrence rate is high, particularly in patients who smoke. In light of this information, it may be time to abandon the standard approach and consider removing all the hardware at the time of infection, clearing the infection, and treating the nonunion once the infection has cleared. In cases in which the hardware is left in place until the fracture is healed, surgeons should strongly consider hardware removal to lower the risk for recurrent infection.

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