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Timing of Antibiotic and Wound Debridement: Does it Matters in Open Fractures of Long Bones.

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Abstract

Background: Open fractures are known to have a multitude of complications. In general, open fractures have been considered as a surgical emergency and treated accordingly with emergency debridement and fixation. Previous animal studies emphasized the need for early debridement and antibiotic administration. However, similar results are not observed and translated in the clinical setting. Hence, we designed an observational study in which our aim was to evaluate the factors which determine union and infections following open long-bone fractures.

Materials and Methods: This is a retro prospective study conducted in a tertiary care hospital from 2015 to 2017. All the open fractures of long bones presented to the casualty not later than 48 h of the injury who were skeletally mature included in the study after obtaining informed consent. All the patients who were presented with the open long-bone injuries were treated as per the institution protocol. Patients were followed up regularly and evaluated.

Results: 59 patients with 69 open fractures were considered for the analysis. Type IIIB and C open fractures were significantly more common in lower-limb injuries. There was no significant difference found between the mean age, gender, involved limb, affected side, presence of the comorbidities, mean time between the injury and the presentation, mean time between injury, and the start of the antibiotics between infected/non-infected and united/non-united open fractures. High-grade injuries took significantly higher number of procedures and time to achieve wound closure. Furthermore, cases with infection and non-union have taken significantly more number of procedures to achieve wound closure. An associated bone loss had a significant increase in the infection, bone grafting, and non-union.

Conclusion: In our study, we noted that open fracture severity and bone loss are the main factors which determine the chances of culture-proven infection. Early antibiotics and wound debridement will not necessarily translate into a decrease in infection rates and non-union.

Keywords: Open fractures, non-union, osteomyelitis, infection, long-bone fractures, bone grafting, soft-tissue injuries.

Introduction

Open fractures are known to have a multitude of complications and hence also have implications on the decision regarding the management of fracture [1, 2, 3, 4, 5]. Since long, open fractures have been considered as the surgical emergency and treated accordingly with emergency debridement and fixation. There are conflicting reports in the literature regarding the cutoff point for the time frame within which if treated; will lead to the decrease in the complications [6-13]. There are innumerable factors of which many are not under the control of physician such as the demographic profile of the patient, nature of the soft-tissue and bone injury, physiological status of the patient, and comorbidities [9, 12]. There are few factors which are deemed to be under the control of treating physician which may not be the case always as in; time since injury, administration of antibiotics, time to debridement, temporary or definitive fixation, and achieving soft-tissue cover [9].

Randomized control studies are ideal to arrive at the conclusion regarding the influence of the time factor in the management of open fractures. Due to the ethical constraints, such studies are not feasible in humans and hence not

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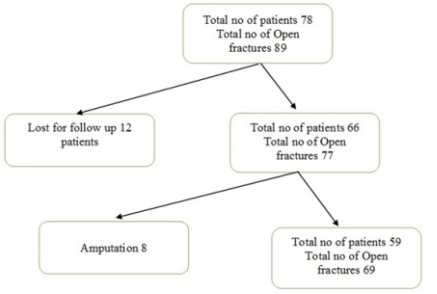

Figure 1: Flowchart showing the number of included patients.

available in the literature. Animal studies have emphasized the need for early debridement and antibiotic administration [8, 14, 15]. However, similar results are not observed and translated in the clinical setting [6, 7, 11, 16, 17]. Hence, we designed an observational study in which our aim was to (1) evaluate the factors which determine the primary outcome variables, namely infections and non-union following open injuries and (2) to evaluate the factors which determine the secondary outcome measures, namely requirement of the bone grafting and number of procedures required before achieving the soft-tissue cover.

Materials and Methods

This is a retro prospective study conducted in the tertiary care and referral hospital from 2015 to 2017. All the open fractures of long bones presented in the emergency who were skeletally mature were included in the study after obtaining informed consent. Patients who were having pathological fractures, surgically treated elsewhere before presentation, and skeletally immature patients were excluded from the study. Institutional ethical committee clearance was obtained for the study.

All the patients who presented with the open long-bone injuries were treated as per the ATLS protocols. Thorough wound wash was given with the copious amount of the saline, and a sterile dressing was done followed by temporary immobilization by malleable splints [18]. An intravenous antibiotic was administered as early as possible. Patients were taken up for the emergency debridement. Open wounds were graded as per the Gustilo–Anderson classification after wound debridement [19]. Depending on the severity of the injury, fractures were temporarily fixed with externa fixator, IM nailing, plating, or screw fixations (Table 1). The decision regarding the primary wound closure was taken on the table after evaluating the soft-tissue injury, contamination, and tissue cover. Redebridement was carried out at 48 to 72 days of interval till definite fixation or wound was deemed suitable for secondary closure, flap cover, or split-skin graft.

Patients were followed up at 6 weeks', 3 months', 6 months', and 12 months' interval. Fracture union was evaluated radiologically RUST (Radiographic Union Scale in Tibial Fractures) criteria. [20,21,22]. Infection was considered after confirmation with deep wound culture swabs. Radiological data were retrieved using the PACS. Surgical data and other relevant details were retrieved from the patient medical records.

Statistical Analysis

The occurrence of the infection, requirement of the bone grafting, and union at the end of the 12 months as per the RUST criteria were the outcome variables. Patient age, the time between injury and presentation, between injury and administration of antibiotics, between injury and debridement, between injury and wound closure, number of procedures before wound

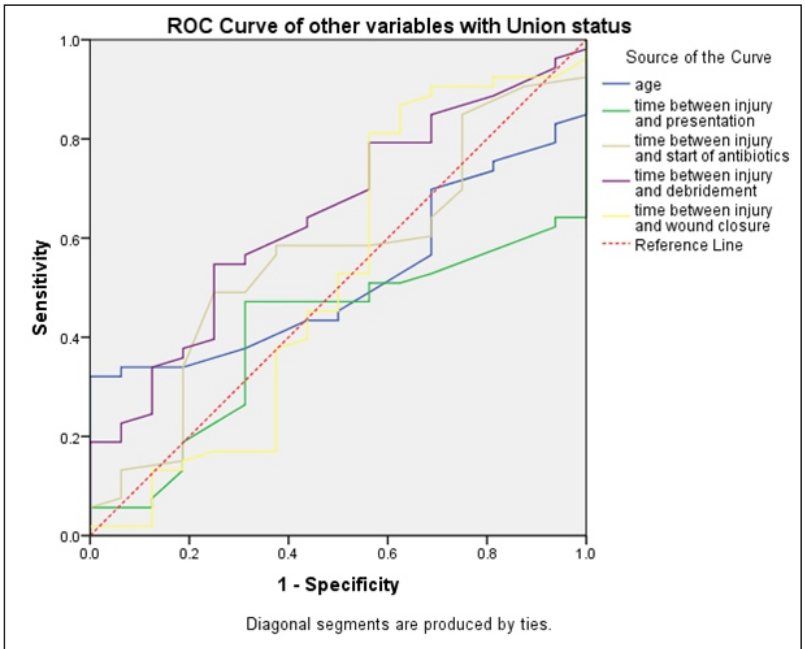

Figure 2: Receiver operating characteristic analysis showing the effect of age and time variable on fracture union status.

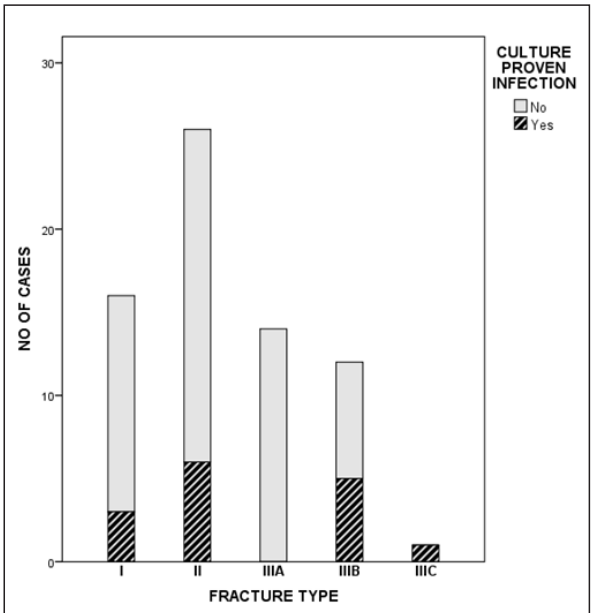

Figure 3: Graph showing open fractures and infection in each Gustilo and Anderson's open fracture classification.

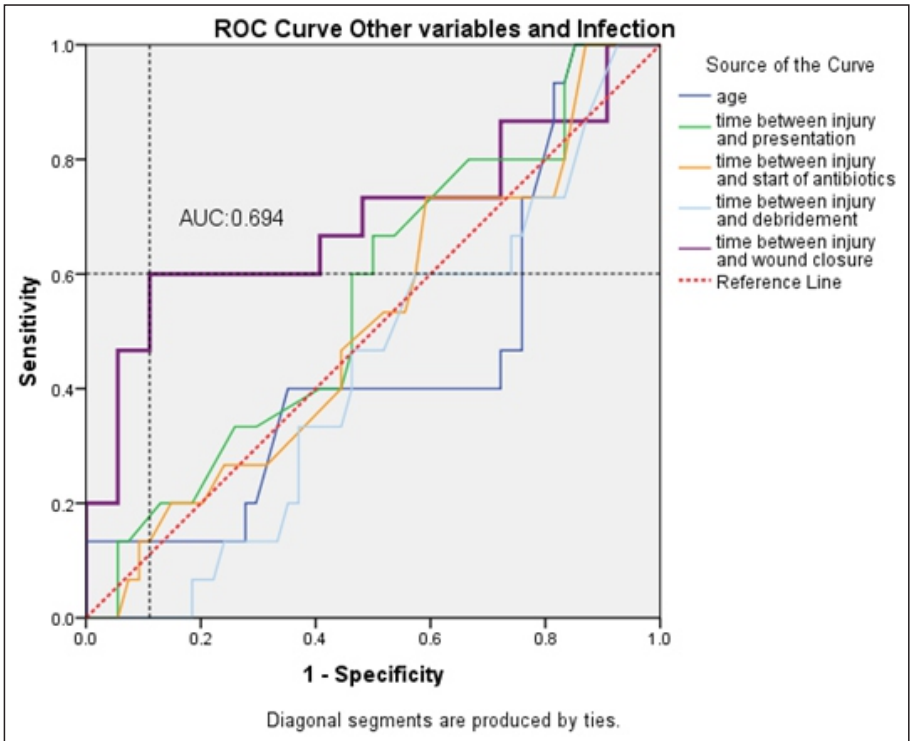

Figure 4: Receiver operating characteristic analysis showing area under the curve 0.694 with P< 0.05 for time to wound closure cutoff value 13025 min.

closure, and RUST score at the end of the 6 months and 12 months were the continuous variables. Gender, affected side, involved limb, presence of bone loss, and presence of comorbid condition were the categorical variables. Converting the continuous variables into categorical variables gave adequate numbers to compare the groups depending on the outcome. Independent sample student t-test was used to compare the means of continues variables. Chi-square test was used for comparing the categorical variables. Receiver operating characteristic (ROC) curve was plotted for continuous variables having significance to find the cutoff value. Statistical analysis was done using SPSS v 20.0 IBM Corporation.

Results

During the study period, 78 patients with 89 long-bone open fractures were enrolled in the study. 66 patients were available for the follow-up after 12 months. Among the available 77 open fractures, 8 underwent amputations. Hence, 59 patients with 69 open fractures were considered for the analysis (Fig. 1).

There were 50 patients with a single open fracture, 8 patients with 2 open fractures, and 1 patient with 3 open fractures. Mean age of the patients was 42.17±16.19 years. The majority were male having involvement of the right lower limb following road traffic accidents. Most common long bones involved were of the tibia followed by femur, forearm, and humerus. High-grade Type III open fractures were significantly more common in lower-limb injuries (P = 0.006). There was no significant difference in the age distribution, the time between injury and presentation, injury and antibiotic administration, and wound debridement between low-grade and high-grade open fractures. High-grade injuries Type IIIB and IIIC took significantly more number of procedures and time to achieve wound closure in comparison to low-grade open injuries (Table 1).

There was no significant difference found between the mean age, gender, involved limb, affected side, presence of the comorbidities, mean time between the injury and the presentation, mean time between injury, and the start of the antibiotics between infected/non-infected and united/non-united open fractures (Fig. 2). The proportion of the infected and non-union cases increased as the severity of the open injury (Table 2 and Fig. 3).

Wound debridement was done significantly early in infected and non-union cases. Furthermore, cases with infection and non-union have taken significantly more number of procedures to achieve wound closure. Infected cases took significantly less time to achieve wound closure (Table 3 and Fig. 4). An associated bone loss had a significant increase in the infection, bone grafting, and non-union. Culture proven infection is significantly associated with non-union status (Table 4).

In our series, we had a preponderance of lower-limb injuries. Upper-limb injuries are more likely to have low-grade injuries, needed less number of surgeries, less bone grafting and less deep infection, and non-union. This despite the fact that there was significantly more delay in taking up for the debridement when compared to lower-limb injuries.

Discussion

Open fractures are most commonly occur due to high-energy trauma. Breeching of the soft-tissue cover and stripping of the soft tissue from the bone disrupt the blood supply and consequent healing problems. Gustilo–Anderson classification still holds good in classifying these injuries. This classification can predict the outcome and complications and hence has prognostic value [3, 4, 19]. Friedrich's with his classic study way back in 1898 on guinea pigs set a rule of "6 hours" beyond which bacterial multiplication will lead to the critical infective load in the open wound [8, 16, 19]. This rule had been endorsed by eminent orthopedic associations until recently [7, 8, 16]. It has been a dictum that open injuries are considered as surgical emergencies and to be debrided arbitrarily within 6 to 8 h

Table 1: Demographic and surgical profile		
Variables	All patients	
Total numberof open fractures	77	
Number of patients	66	
Male/Female	62/4	
Age	40.38±16.40 years	
Affected limb		
Right/Left	38/28	
Mechanism of injury		
RTA	55	
Fall	7	
Others	4	
Amputation		
Yes	8	
No	69	
Total fractures	69	
Single Open fracture	50	
Two Open fractures	8	
Three Open fractures	1	
Number of Patients at Final Followup	59	
Male/Female	55/4	
Age	42.17(±16.19) years	
Affected limb		
Right/Left	44/25	
Affected limb		
Upper/Lower limb	14/55	
Involved bone		
Humerus	6	
Forearm	8	
Femur	16	
Leg	39	
Surgery done		
Nailing	34	
Plating	25	
Screws	2	
External fixator	3	
Non-Op	5	
Associated bone loss		
Yes	12	
No	57	
Bone grafting		
Yes	7	
No	62	
Time of presentation	292.83 (±308.29) (15–1510) min	
<6 h	50(72.5%)	
>6 h	19(27.5%)	
Antibiotic	640.58 (±944.76) (60–6000) min	
< 6 h	32(46.4%)	
>6 h	37(53.6%)	
Debridement	1816.23 (±2576.48)(270–14100) min	
<24 h	49(71.0%)	
>24 h	20(29%)	
Wound Cover	8127.75(±11279.30)(450–70080) min	
<5 days	45(65.2%)	
>5days	24(34.8%)	
Comorbidities		
Yes	16(23.2%)	
No	53(76.8%)	
Infection		
Yes	15(21.7%)	
No	54(78.3%)	
Union Status	In 6 months	In 12 months
United	36(52.2%)	53(76.8%)
Not/Delayed Union	33(47.8%)	16(23.3%)
Number of surgeries before skin closure	1.78 (±0.953) (1to 4)	
RUST score		
At 6 months	9.09(±2.68)	
At 12 months	10.42(±2.36)	

Table 2: Open fracture classification and outcome			
Open fracture classification	In no	Infected	Not united
I	16	3 (18.8%)	2(12.5%)
II	26	6(23.1%)	6(23.1%)
IIIA	14	0(0%)	4(28.6%)
IIIB	12	5(41.7%)	3(25%)
IIIC	1	1(100%)	1(100%)
Total	69	15	16

so as to reduce the complications such as infection and non-union. However, these recommendations have been questioned by recent studies [6, 7, 8, 11, 13, 16, 17, 19].

Majority of our patients were male (62/66) who sustained injury commonly due to RTA while driving a motorcycle [19]. Involvement of right lower limb was common due to the left lane driving conditions, which is seen in other studies also [23]. Bone grafting was needed more often for the right-sided injuries which could be explained due to the severity of the injury sustained by direct impact during RTA.

Being a developing country, lack of proper infrastructure and evolving pre-hospital care, we have noted wide variation in time taken for the presentation to our tertiary care center. Although not statistically significant, it is curious to note that patients with high-grade injuries have reached hospital earlier than low-grade injuries. Due to socioeconomic and other factors, high-grade injuries are taken to tertiary care centers directly, whereas low-grade non-life-threatening injuries are taken first to nearest primary or secondary health-care facilities and later shifted to tertiary centers which lead to delay in presentation.

Similarly, high-grade injuries received early antibiotics and debrided much earlier than low-grade injuries which were though not significant when compared to low-grade injuries. This also could be due to preferential treatment received by high-grade injuries in the trauma triage and during allotment of emergency OT [12]. Such delay due to infrastructural constraint has been observed by Spencer et al. as well [7]. As expected high-grade injuries needed significantly more number of surgeries, took more time to achieve skin cover and more likely to get infected.

On the contrary to the expectation, cases which got infected and went into the non-union had undergone wound debridement earlier than other fractures, suggesting earlier wound debridement is not the only factor leading to better outcome [12]. Hull et al. in their study noted the relatively small increase (3%) in the odds ratio for infection for every hour of delay. However, he also has noted that other factors such as the grade of an open fracture, site of injury, and gross contamination have much more impact on the infection [12]. Furthermore, higher the number of surgical interventions needed before the skin cover despite achieving early soft-tissue cover and presence of bone loss; chances

Table 4: Effect of the different categorical variable on the outcome				
Parameter	Infection	Bone grafting	Union status at 6	Union status at 12
Gender (male/female)	0.871	0.489	0.346	0.93
Limb Involved (upper/lower)	0.449	0.159	0.106	0.111
Affected side (right/left)	0.792	0.035*	0.327	0.097
Open Type (I, II, IIIA/IIIB, IIIC)	0.018*	0.745	0.893	0.472
Soft-tissue injury (Y/N)	0.544	0.453	0.83	0.158
Associated Bone loss (Y/N)	0.001*	0.000*	0.000*	0.000*
Time of presentation (<6h/>6 h)	0.57	0.338	0.622	0.704
Antibiotic(<6h/>6 h)	0.98	0.547	0.737	0.14
Debridement (<24 h/>24 h)	0.131	0.075	0.058	0.097
Wound closure (<5 days/>5 days)	0.020*	0.716	0.441	0.795
Comorbidities (Y/N)	0.718	0.722	0.71	0.631
Infection	NA	NA	0.005*	0.000*
*P <0.005 (Chi-square test)				

Table 3: Age and different time factors on the injury and outcome

Effect of	Type I,II,IIIA	Type IIIB, IIIC	sig	Infected	Not infected	Sig	United	Not United	Sig
Age in years	42.05±15.844	42.69±18.309	0.899	39.67±18.38	42.87±15.65	0.502	42.51±17.49	41.06±11.25	0.698
Time between injury and presentation in min	299.11±317.35	265.77±275.62	0.728	323.00±306.66	284.44±311.07	0.672	285.57±315.50	316.88±291.4	0.715
Time between injury and start of antibiotics in min	688.84±1035.66	432.69±290.20	0.382	513.00±348.90	676.02±1052.21	0.558	697.26±1058.50	452.81±336.58	0.368
Time between injury and debridement in min	1967.86±2817	1163.08±812.67	0.314	1023.00±615.50	2036.57±2861.71	0.019*	2089.72±2871.05	910.31±614.98	0.007*
Time between injury and wound closure in min	5683.13±10308.94	18658.46±9263.46	0.000*	16977.00±5669.63	18652.59±6557.94	0.036*	7828.11±11315.82	9120.31±11466.31	0.695
Number of surgeries before skin closure	1.46±0.68	3.15±0.68	0.000*	2.80±0.94	1.50±0.74)	0.000*	1.66±0.919	2.19±0.98	0.068

*Unpaired student *t*-test (p<0.05)

of infections are significantly higher (Fig. 4) [9] which implies that chances of infection are dependent on the severity of tissue injury and bone loss. Hence, many authors have started questioning the 6 h rule and to take up the open cases during unofficial hours to operation theater, having tired and inexperienced medical personnel, without proper surgical plan leading to suboptimal debridement and fixations [19]. With similar findings, we are also of the opinion that it is better to embark on managing the complex open fractures during daytime when all the facilities and expertise will be at the surgeon's disposal. We are of the opinion that, planned proper debridement and ending up in planned definitive fixation are the way to get the better outcome.

In our study, we have utilized RUST fracture scoring for evaluation of union using radiographs in two views and consider 4 cortex healing [21]. Each cortex receives score 1 if there is no callous. If callous seen and fracture line is visible, then score 2 will be given. If fracture is healed and fracture line is not visible, then it will be given score 3. Hence, maximum of 12 score suggests complete fracture healing and minimum of 4 score suggests no fracture healing. RUST scoring was developed mainly for tibial fractures [20]. It has been used for other fracture union prediction as well [22]. RUST scoring has been validated and found to have moderate-to-good inter and intraobserver agreement [20, 21]. Hence, we have extrapolated the same score in other long bones as well. The bone loss which results in an inability to maintain cortical continuity is found to be associated with significantly with non-union which is also observed earlier by Fong et al. [24]. In our study, we observed that the proportion of the fractures which go for non-union at the end of the 12 months increases as the open fracture grading increases, which is expected as the severity of the soft-tissue disruption and fracture pattern increases; healing will be delayed. Similarly, we observed that the proportion of fracture going for the infection also increases depending on the severity of the open injury grading except for IIIA. Many fractures with intact soft-tissue envelope but small wound (<1 cm) having nil to minimal contamination would be classified into Grade IIIA due to comminution, which might be the reason for such aberration. This finding is in line with the previous studies refuting the claim of early debridement which would lead to a better outcome [4, 6, 16, 24].

In our series, upper-limb injuries fared much better when compared to lower-limb injuries. This could be because of the fact that they are less frequent, are of lower grade, and in general, they have very good soft-tissue cover, when compared to leg injuries which are much more common. A similar trend has been observed by many authors [6].

We observed that the number of procedures which were needed before achieving soft-tissue cover is a significant predicting factor for forthcoming infection, non-union in a high-grade fracture despite early soft-tissue cover. Webb et al. arrived at the similar conclusion in their study on analysis of surgeon-controlled factors in Type III open tibial fractures [9]. Based on our observations, we recommend surgical planning which will have a minimum number of interventions to achieve the earliest definitive fixation and soft-tissue cover. This strategy was found to be successful by Rajasekaran et al. in their study on immediate primary skin closure in Type IIIA and Type IIIB open fractures in carefully selected patients [25].

Prospective nature of the study with accurate documentation of chronological events which happens in the busy trauma clinical setting with good follow-up is the strengths of our study. Not including complexity of the fracture pattern explicitly could be considered as a weakness in this study. However, Grade IIIA can act as representative for complex fracture which includes comminuted and segmented fracture patterns [16].

Conclusion

In our study, we noted that open fracture severity and bone loss are the main factors which determine the chances of culture-proven infection. The presence of infection and bone loss predisposes to non-union. Early antibiotics and wound debridement might not necessarily translate into reduction in infection and non-union rates in open long-bone fractures.

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