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ORIGINAL PAPER

A review of forty five open tibial fractures covered with free flaps. Analysis of complications, microbiology and prognostic factors

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Abstract
Purpose Treatment of open fractures is complex and controversial. The purpose of the present study is to add evidence to the management of open tibial fractures, where tissue loss necessitates cover with a free flap. We identified factors that increase the risk of complications. We questioned whether early flap coverage improved the clinical outcome and whether we could improve our antibiotic treatment of open fractures.
Methods From 2002 to 2013 we treated 56 patients with an open tibial fracture covered with a free flap. We reviewed patient records and databases for type of trauma, smoking, time to tissue cover, infection, amputations, flap loss and union of fracture. We identified factors that increase the risk of complications. We analysed the organisms cultured from open fractures to propose the optimal antibiotic prophylaxis. Follow-up was a minimum of one year. Primary outcome was infection, bacterial sensitivity pattern, amputation, flap failure and union of the fracture.
Results When soft tissue cover was delayed beyond seven days, infection rate increased from 27 to 60 % (p<0.04). High-energy trauma patients had a higher risk of amputation, infection, flap failure and non-union. Smokers had a higher risk of non-union and flap failure. The bacteria found were often resistant to Cefuroxime, aminoglycosides or amoxicillin, but sensitive to vancomycin or meropenem.
Conclusion Flap cover within one week is essential to avoid infection. High-energy trauma and smoking are important predictors of complications. We suggest antibiotic prophylaxis with vancomycin and meropenem until the wound is covered in these complex injuries.

Keywords Open tibial fractures · Antibiotics · Infection · Microbiology · Timing · Free flap · Amputation · Smoking

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Introduction

Open fractures have an increased risk of infection and non-union. These complications may result in amputation and septic shock. The most severe cases, with significant soft tissue injury, need both osteosynthesis of the bone and a plastic surgical procedure, in the form of a free flap, to restore the soft tissue. Furthermore, the fragile soft tissue mantle in the distal tibia and the lack of reliable local flaps in this area is a challenge for orthopaedic and plastic surgeons. The ultimate goals of the treatment are to avoid amputation and infection, restore soft tissue cover and achieve union of the fracture (Figs. 1, 2 and 3).

The literature remains inconclusive on the topic of antibiotic treatment and timing of soft tissue cover, probably due to the relatively small number of patients in each centre with this

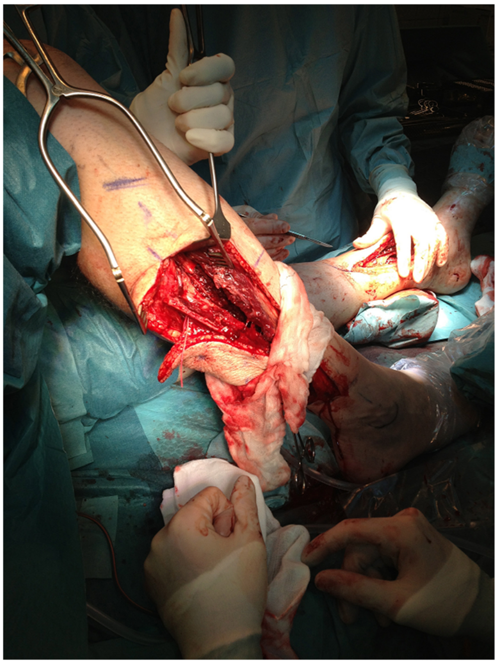

Fig. 1 A free fibula graft with muscle and skin from the right leg of the patient, is transferred to the left side, where the patient sustained an open distal tibial fracture, with substantial bone loss

Fig. 3 6 months after. Donor and the graft site. The patient is walking unaided, with no pain

condition [1–5, 7–9]. Furthermore, hospital logistics may delay the most optimal course. The delay in time to skin cover is probably rooted in a lack of consensus on timing, different approaches to the treatment of severely injured patients with other life or limb-threatening injuries and lack of capacity. In our hospital, the delay in flap coverage was rooted in a capacity problem; typically, an elective tumour patient operation must be cancelled for the microsurgery team to operate on an open fracture patient.

The purpose of our study was to investigate the determining factors that reduce the risk of amputation, infection and nonunion and to identify relevant first-line antibiotics. We believe that our study is unique in its combination of data on microbiology and timing of cover of open fractures. These aspects have not previously been discussed in the same context, although they are closely associated.

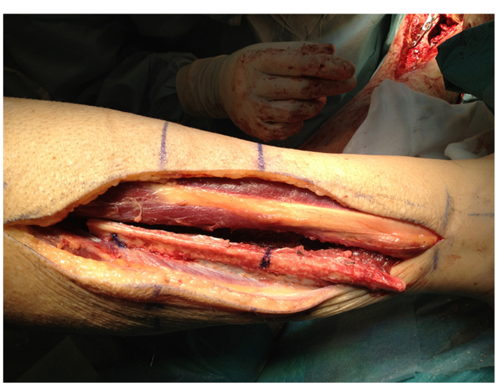

Fig. 2 The fibula is exposed

Methods

This study was conducted at the Department of Orthopaedic Surgery and Trauma and at the Department of Plastic Surgery, Copenhagen University Hospital, Rigshospitalet, Denmark. Rigshospitalet is a referral centre for fractures with soft tissue loss and has a catchment population of 1.7 million.

The study included all patients with open fractures of the tibia, covered with free vascularized flaps at our institution from January 2002 to June 2013. Patients with initially closed fractures and patients with chronic osteomyelitis were excluded. The patients included in the study were identified from our database of all microsurgical procedures conducted by the Department of Plastic Surgery during the period.

We retrospectively collected data from patient records (history, tobacco use, fracture type, fracture union, timing of surgical procedures, flap failure, infection, amputation) and from our local microbiological database (samples, species, antibiotics, susceptibility patterns) and from the microsurgical database (flap types, timing).

Injury type was recorded according to Müller-OTA fracture classification and the Gustilo-Anderson soft tissue damage classification [1, 12]. Initial wound treatment was classified as “Open” when negative pressure wound therapy (NPWT), or any other type of open dressing was used. “Closed” wound treatment denoted cases where primary suturing of the wound proceeded to wound breakdown and necrosis. We defined infection when CRP and/or white cell count was elevated in combination with pus, discharge or wound breakdown, provided it was related to the initial lesion, including the flap. Superficial signs of infection and external fixator pin tract infections were excluded. Positive cultures or blood tests without clinical signs of infection were not included.

Union of the fracture was evaluated radiographically and we defined non-union when less than three out of four cortices had bridging callus in anteroposterior and lateral views, one year or later, after initial surgery. High-energy trauma was defined as: polytrauma in general, including falls from a height of ≥2.5 m, motor vehicle or motorcycle accidents, bicycle accidents, pedestrians being hit by any of the above and crushing injuries. Low-energy trauma was defined as fall from standing height or up to < 2.5 m or other low-impact injuries.

The bacterial species isolated from the wounds and their susceptibility patterns were defined with respect to time from injury. We included sample cultures between the second and 30th day after injury. Cultures from initial wound revisions were not included. This avoided the early wound contamination period (which has previously been shown to have poor correlation with later infection pathogens) [22, 23]. The samples included were biopsies harvested from deep tissue during surgical wound revisions of patients that were clinically infected. Blood-, pin site- and catheter cultures were not included. Identical results were counted only once. The susceptibility of identified microorganisms to relevant antibiotics was tested by disc diffusion. We included only positive samples that were fully susceptible to the antibiotic tested.

We used Fischer’s Exact test for dichotomous variables and set the level of significance at $p=0.05$. We calculated the relative risk ratio for each outcome measure related to the energy of initial trauma. Clinical follow-up was a minimum of one year for all patients.

Results

From January 2002 until June 2013, 56 patients received a free vascularized flap to cover an open fracture of the tibia at our institution. Of these, 11 had insufficient or irretrievable patient records, leaving 45 patients to be included in the study. The patients with irretrievable records were all from the period (2002–2005), prior to the introduction of electronic patient records.

The study group consisted of 13 women and 32 men. The average age was 42 years (range 16–71, SD 18). Gustilo Anderson type IIIB fractures accounted for 26 (57 %) of the lesions, and six (13 %) were Gustilo Anderson IIIC. Thirty-one patients (67 %) sustained high-energy trauma. There were 15 smokers (33 %). One patient had bilateral fractures.

All patients were initially debrided with copious lavage. The average time to first debridement was 6.8 hours (range one to 26, SD 6.2). After debridement 31 patients (67 %) with 32 fractures continued with open wound care, typically with negative pressure wound therapy (NPWT). The remainder (15) had closed wound therapy with sterile dressings and suturing of the wound, that later went on to wound breakdown.

Sixteen patients were primarily stabilized with internal fixation (plates, nail or screws). The remaining 29 patients were treated with temporary external fixation, which was converted to internal fixation in combination with the free flap.

The average time to flap cover was 16 days (range two to 54 days, SD 13, excluding one outlier at 450 days). The free flaps consisted of 24 latissimus dorsi flaps, 13 gracilis flaps, three vascularized free fibulas, five anterolateral thigh flaps (ALT) and a single radial forearm flap. One patient had flaps to both tibias (patient no. 7) (see Table 1).

Infection Twenty-two fractures (48 %) became infected at an average of 21 days from the initial trauma (range four to 83 days, SD 21 days, excluding an outlier at 360 days). In the group receiving flap cover before day seven (early cover), five out of 18 became infected (27 %), and in the group of patients receiving the flap after day seven (late cover), 17 out of 28 became infected (60 %). The difference between infection rates in the two groups was statistically significant ($p<0.04$).

Non-union Nineteen (41 %) fractures were not united one year after osteosynthesis. Non-union occurred in ten out of 16 patients in the smoking group (63 %), compared to nine out of 30 patients (30 %) in the non-smoking group. The difference between non-union rates in the smoking and the non-smoking group was almost significant ($p<0.058$).

Limb salvage In four patients (9 %), continuing infection required treatment with a below the knee amputation. Two of these had an infected non-union. Mean time to amputation was 17.2 months (0.4, 14, 14 and 40 months). The association between amputation and infection was statistically significant ($p<0.04$).

Flap failure Seven patients (19 %) sustained partial or complete loss of the free flap, resulting in a secondary procedure. None of these patients were amputated and all of them underwent either successful repair or replacement of their flaps. Flap failure was significantly associated with smoking, with five out of seven (71 %) flap failures occurring in the smoking group ($p<0.04$).

Table 1 Patient demographics

Patient	Age	Year	Smoker	Fracture	GA class	High energy	Wound treatment	Flap type	Stabilization	First debridement (hours)	Final cover (days)	Infection	Flap failure	Amputation	Non-union
1	43	2005	Yes	44A	GA3B	Yes	Open	LD	Plates	24	8	Yes	Yes	No	No
2	39	2009	No	42A	GA3B	Yes	Open	ALT	ex fix	17	5	No	No	No	Yes
3	43	2013	Yes	41C3	GA3B	Yes	Open	LD	Plates	3	4	Yes	No	Yes	Yes
4	25	2012	No	42C3	GA3C	Yes	Open	LD	Plates	11	3	Yes	No	Yes	No
5	72	2011	No	42A	GA3B	Yes	Open	Grac	ex fix	?	27	No	No	No	No
6	45	2002	Yes	42A3	GA3B	Yes	Closed	LD	ex fix	12	22	Yes	No	No	Yes
7	71	2011	No	42B1	GA3B	Yes	Open	LD	ex fix	4	15	No	No	No	No
7	71	2011	No	42A2	GA3B	Yes	Open	LD	ex fix	4	15	No	No	No	No
8	22	2008	Yes	42A3	GA3B	Yes	Open	LD	ex fix	2	15	Yes	No	No	Yes
9	44	2012	No	41C3	GA3B	Yes	Open	LD	Plates	3	13	Yes	No	No	Yes
10	49	2011	No	42B2	GA3C	Yes	Open	LD	Plates	3	12	Yes	Yes	No	Yes
11	52	2011	No	44B3	GA3B	Yes	Open	ALT	Plates	4	9	No	No	No	No
12	16	2005	Yes	42A3	GA3B	No	Open	LD	ex fix	4	5	No	No	No	No
13	46	2012	Yes	44BC	GA3B	Yes	Open	LD	Plates	4	5	No	No	No	Yes
14	39	2009	Yes	43B2	GA3A	No	Open	Grac	ex fix	6	450	Yes	Yes	No	Yes
15	27	2011	No	41A1	GA3B	No	Open	LD	Plates	4	2	No	No	No	No
16	61	2007	No	42C1	GA3B	No	Closed	Grac	Plates	0	24	Yes	No	No	No
17	59	2007	Yes	43C3	GA3B	Yes	Closed	LD	ex fix	12	21	Yes	No	No	Yes
18	35	2010	No	42B2	GA3B	No	Open	Grac	Nail	1	6	No	No	No	No
19	31	2005	No	43B2	GA3B	Yes	Closed	Grac	Plates	5	41	Yes	Yes	No	Yes
20	17	2006	No	42C1	GA3B	Yes	Closed	Grac	ex fix	2	7	No	No	No	Yes
21	38	2011	No	42A1	GA3A	No	Open	ALT	ex fix	7	18	No	No	No	Yes
22	80	2011	No	44B2	GA3A	No	Open	Radialis	ex fix	5	22	No	No	No	Yes
23	64	2010	No	43C3	GA3C	Yes	Open	ALT	ex fix	6	6	Yes	No	Yes	No
24	30	2009	Yes	43B2	GA3C	Yes	Open	LD	ex fix	8	6	Yes	No	No	Yes
25	29	2004	Yes	42A2	GA2	Yes	Closed	LD	ex fix	24	30	Yes	No	No	Yes
26	34	2005	Yes	42B2	GA2	No	Closed	LD	ex fix	12	17	No	No	No	Yes
27	77	2012	No	44B2	GA3B	No	Open	LD	ex fix	3	6	Yes	No	No	No
28	59	2012	No	41A3	GA3B	Yes	Closed	LD	ex fix	17	18	Yes	No	No	No
29	24	2003	Yes	44B1	GA3B	Yes	Open	LD	Cast	2	6	No	Yes	No	No
30	56	2007	Yes	42C2	GA2	Yes	Closed	Grac	ex fix	12	54	No	Yes	No	No
31	67	2011	No	44C1	GA2	No	Open	LD	ex fix	3	50	Yes	No	No	No
32	21	2010	No	43A3	GA3C	Yes	Open	Fib	ex fix	12	13	No	No	No	No
33	42	2009	No	43B2	GA3B	Yes	Open	LD	ex fix	4	6	No	No	No	No
34	56	2013	No	41C1	GA3B	Yes	Open	alt	Plates	26	16	yes	No	No	No

Table 1 (continued)

Patient	Age	Year	Smoker	Fracture	GA class	High energy	Wound treatment	Flap type	Stabilization	First debridement (hours)	Final cover (days)	Infection	Flap failure	Amputation	Non-union
35	41	2005	No	42C3	GA3B	Yes	Open	Grac	ex fix	6	7	No	No	No	No
36	35	2002	Yes	42B2	GA2	Yes	Closed	LD	ex fix	1	39	No	Yes	No	Yes
37	67	2012	No	43B3	GA3B	No	Open	Fib	ex fix	9	5	No	No	No	No
38	15	2002	No	44B3	GA2	No	Closed	Grac	ex fix	8	41	No	No	No	No
39	42	2005	No	42A2	GA3A	Yes	Closed	LD	Nail	5	31	Yes	No	No	No
40	22	2013	No	43B2	GA2	No	Open	Grac	Screws	2	5	No	No	No	No
41	16	2002	No	42A2	GA3B	Yes	Closed	Grac	ex fix	6	30	Yes	No	No	No
42	19	2009	No	44C2	GA3A	Yes	Closed	LD	Plates	8	16	Yes	No	Yes	Yes
43	29	2009	Yes	42C3	GA3C	Yes	Open	Fib	ex fix	6	3	No	No	No	No
44	28	2013	Yes	43C2	GA1	No	Closed	Grac	Plates	9	37	Yes	No	No	No
45	35	2012	No	42B3	GA2	No	Open	Grac	ex fix	8	7	No	No	No	Yes

Fracture type according to AO

LD Latissimus dorsi; *ALT* anterolateral thigh; *Grac* Gracilis; *Fib* fascio-myocutaneous fibula flap; *GA* Gustilo-Anderson classification; *Ex fix* external fixation

Injury severity All four patients who were amputated were in the high-energy trauma group. Seventeen of 22 infected patients (77 %) were in the high-energy group. Furthermore, six out of seven (86 %) flap failures and 14 of 19 (74 %) non-union cases were in the high-energy group. When comparing high-energy trauma with low-energy trauma, the relative risk ratios for amputation, flap failure, infection and non-union were 3.8, 2.9, 1.6 and 1.4, respectively.

Culture results We isolated 43 different bacterial species in 22 infected patients from day two to 30. Six of the infections were monomicrobial, nine had two different bacteria and the rest were polymicrobial. Seven bacteria accounted for 75 % of the infections, enterococcus species and coagulase negative staphylococcus (CoNs) being the most frequent. The patterns of sensitivity are seen in Table 2.

Discussion

The importance of timing of cover in open fractures has been investigated by a number of authors, most notably Godina, who was the first to report the importance of early skin cover to reduce the risk of infection [19]. Later, a number of other observers have come to similar conclusions, but many other aspects of trauma care may also play a role in preventing infection and securing union in these injuries.

Alleuyrand et al. found that patients receiving flap cover before day seven had a better outcome in terms of flap failure and infection, even when controlling for known risk factors such as severity of trauma [2]. Choudy et al. also found a higher non-union rate and infection rate in patients with flap cover after day seven [20].

Gopal et al. and Sinclair et al. reported series of open tibial fractures with very early skin cover (before day three) and definitive stabilization; 90–95 % of these patients had successful flap cover, with no infection, union of the fracture and excellent outcome without pain or walking disability [4, 5]. Such results are exceptional. In another series, infection rates, flap failure rates and non-union rates exceed 30–50 %. Other authors, in line with the guidelines of the British Orthopaedic Association, have reached similar conclusions, albeit at various breakpoints [2–5, 7–11].

Our study sample size did not permit a multivariate analysis of all possible confounders, but it confirmed unequivocally that patients covered before day seven had a significantly lower infection and non-union rate, irrespective of trauma degree.

These results should encourage surgeons to strive for an ortho-plastic service enabling rapid free-flap cover and definitive stabilization within one week after trauma. We

Table 2 The number of cultures fra infected wounds and their sensitivity pattern

Bacteria	Number	Vanco	Mero	Linez	Genta	Sulfa	Amp	Moxi	Ery	Rif	Cipro	Cefur	Azit	Metro
Enterococcus species	11	11	7	9			9	5	5	1		0	2	
Coagulase neg. staphylococci (CoNS)	9	9		9	5			3	2	8		3	3	
Enterobacteriaceae	6		5		5	5	1				5	1		
Miscellaneous	6	5	6	3		5	2	4	2		2	2	2	
Other pseudomonas	4		2		2	3	0				3			
Anaerobic bacteria	2		2					1						2
Staphylococcus aureus	2	2		2	2				1	2		2	2	
Haemolytic streptococci	1	1	1			1	1		1			1		
Corynebacterium species	1	1	0	1		0	0	0	1			0		
Pseudomonas aeruginosa	1		1		1						0			
Total	43	29	24	24	15	14	13	13	12	11	10	9	9	2

Only samples with full sensitivity were included.

Vanco Vancomycin; *Mero* Meropenem; *Linez* Linezolid; *Genta* gentamycin; *Sulfa* sulphonamide; *Amp* Ampicillin; *Moxi* moxifloxacin; *Ery* Erythromycin; *Rif* rifampicin; *Cipro* ciprofloxacin; *Cefur* cefuroxim; *Azit* azitromycin; *Metro* metronidazol

accept that none of these studies are randomized trials of early and late cover, which is a general weakness of the literature.

In our study, flap failure was not a predictor of amputation. This is an important point, also observed by Choudry et al., illustrating that a flap revision or a second flap can often allow limb salvage [20]. At our institution, local muscle flaps are not used for immediate soft tissue cover after lower extremity trauma due to high complication and revision rates [3, 18, 20]. Choudry et al. also found that cover later than one week using soleus pedicled flaps for open tibia fractures resulted in higher nonunion rates, higher flap failure rates and more infection when compared to free muscle flaps [20]. Use of tobacco was a significant predictor of flap failure, a well known problem in plastic surgery, also described by Christy et al., [17]. Hence, smokers with complex injuries should be counseled on quitting smoking.

Patzakis and Wilkins (in 1989) were among the first to observe that immediate antibiotic prophylaxis in patients with open fractures is the single most important factor that will reduce the risk of infections [6]. Furthermore, grade III open fractures in need of tissue cover pose a problem for the clinician. The wound may be open for several days allowing colonization and adherence of selected bacteria that are resistant to the antibiotics given. In line with these observations, it has been shown that cultures obtained at initial debridements correlate poorly with later infections, which is why we only included cultures from patients that were clinically infected, and not cultures from day zero to two [22, 23]. Thus, antibiotic treatment should be broad, target both Gram positive and negative organisms, and the risk of generating resistance should be small [13–16]. The risk can be further reduced by using antibiotics that are renally excreted with minor impact on the normal flora, as proposed by Sullivan et al. [21]. Also, reduced selection for resistant pathogens can be expected due to the reduced time to soft tissue coverage, and the resulting decreased period with need for antibiotic treatment.

Gopal et al., in common with Pollack et al., have proposed the use of Cefuroxime and metronidazole for open tibia fractures. This was the combination of antibiotics used at our institution, but in only 12 of 43 (28 %) cases would these antibiotics have been effective against the bacteria cultured from our patients before flap cover [3, 4].

As depicted in Table 3, vancomycin, which is bacteriocidal, was effective against 29 of 43 isolated cultures and was active against all Gram-positive bacteria identified in the study.

Meropenem was effective against 24 of 43 organisms, with particular effect against the miscellaneous group, enterobacteriacae and other Gram-negative rods, enterococcus and anaerobes. Gentamicin covered 15 of 43 organisms, but none of the important enterococcus species.

Linezolid also covered the Gram-positive organisms in our samples, and has good penetration into tissues, but is only licensed for a limited period of time and is very costly.

Based on these results, we suggest a combination of vancomycin and meropenem as first line antibiotic prophylaxis. In combination, these antibiotics seldom lead to resistance, are generally well tolerated, and supplement each other well. They are both mainly renally excreted. In this series, vancomycin and meropenem would have covered 40 of 43 (93 %) organisms cultured. This has also been demonstrated in a series of 166 patients with chronic osteomyelitis occurring mainly after fracture with internal fixation, in which Sheehy et al. recommended vancomycin and meropenem for empirical initial treatment of the organisms identified at excision of the bone infection [13].

Table 3 Outcome of patient demographics and complications

Outcome	Late cover (61 %)	Early cover	High energy (67 %)	Low energy	Open wound (67 %)	Closed wound	Proximal fracture (59 %)	Distal fracture	Infection (48 %)	No infection	Non smoker (62 %)	Smoker
Amputation (9 %)	1	3	4	0	3	1	2	2	4	0	3	1
No amputation	27	15	27	15	28	14	25	17	18	24	27	15
p-value	0.280		0.290		1.000		1.00		0.044*		1.00	
Infection (48 %)	17	5	17	5	12	10	12	10			13	9
No infection	11	13	14	10	19	5	15	9			17	7
p-value	0.038*		0.217		0.146		0.770				0.54	
Flap failure (15 %)	6	1	6	1	4	3	3	4	4	3	2	5
No failure	22	17	25	14	27	12	24	15	18	21	28	11
p-value	0.220		0.399		0.660		0.424		0.690		0.040*	
Non-union (41 %)	13	6	4	5	11	8	12	7	11	8	9	10
Union	15	12	17	10	20	7	15	12	11	16	21	6
p-value	0.540		0.539		0.340		0.763		0.369		0.06	

* Statistically significant associations are marked with an asterisk

The patterns of resistance may differ geographically and should also be considered in a regional context. We are aware that prophylaxis with broad-spectrum antibiotics could result in unwanted resistance patterns, but this problem should be seen in the light of a very small number of patients presenting with open fractures with compromised soft tissue. However, short duration treatment with effective antibiotic regimes should also minimize the development of resistance and prevent later infection that will inevitably require much longer antibiotic therapy with risks for resistance.

Conclusion

We conclude that a delay in soft tissue cover beyond day seven from the initial trauma is associated with an increased infection and non-union rate. Smoking markedly increases the risk of non-union and flap failure. High-energy trauma increases the relative risk of flap failure, infection, non-union and amputation.

We also conclude that currently proposed antibiotics have limited effect on bacteria infecting grade 3 open fractures.

We have changed the standard antibiotic prophylaxis at our institution to vancomycin and meropenem, thus improving the expected coverage of organisms from 28 to 93 %.

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Conflict of interest No conflicts of interest declared.

References

1. Gustilo RB, Anderson JT (1976) Prevention of infection in the treatment of 1025 open fractures of long bones: retrospective and prospective analyses. J Bone Joint Surg Am 58:453–458
2. D'Alleyrand JC, Manson TT, Dancy L et al (2014) Is time to flap coverage of open tibial fractures an independent predictor of flap-related complications? J Orthop Trauma 28:288–293
3. Pollak AN, McCarthy ML, Burgess AR (2000) Short-term wound complications after application of flaps for coverage of traumatic soft-tissue defects about the tibia. The Lower Extremity Assessment Project (LEAP) Study Group. J Bone Joint Surg Am 82:1681–1691
4. Gopal S, Majumder S, Batchelor AG et al (2000) Fix and flap: the radical orthopaedic and plastic treatment of severe open fractures of the tibia. J Bone Joint Surg (Br) 82:959–966
5. Sinclair JS, McNally MA, Small JO et al (1997) Primary free-flap cover of open tibial fractures. Injury 28:581–587
6. Patzakis MJ, Wilkins J (1989) Factors influencing infection rate in open fracture wounds. Clin Orthop Relat Res 243:36–40

7. Hohmann E, Tetsworth K, Radziejowski MJ et al (2007) Comparison of delayed and primary wound closure in the treatment of open tibial fractures. Arch Orthop Trauma Surg 127:131–136
8. Cierny G 3rd, Byrd HS, Jones RE (1983) Primary versus delayed soft tissue coverage for severe open tibial fractures. A comparison of results. Clin Orthop Relat Res 178:54–63
9. Hertel R, Lambert SM, Müller S et al (1999) On the timing of soft-tissue reconstruction for open fractures of the lower leg. Arch Orthop Trauma Surg 119:7–12
10. Crowley DJ, Kanakaris NK, Giannoudis PV (2007) Debridement and wound closure of open fractures: the impact of the time factor on infection rates. Injury 38:879–889
11. BOAS British Orthopaedic Association (2014) Guidelines for open fractures (BOAST 4). http://www.boa.ac.uk/publications/boast-4-the-management-of-sever-open-lower-limb-fractures/. Accessed 20 Feb 2015
12. Marsh JL, Slongo TF, Agel J et al (2007) Fracture and dislocation classification compendium - 2007: Orthopaedic Trauma Association classification, database and outcomes committee. J Orthop Trauma 21:S1–S133
13. Sheehy SH, Atkins BA, Bejon P et al (2010) The microbiology of chronic osteomyelitis: prevalence of resistance to common empirical anti-microbial regimens. J Infect 60:338–343
14. Hauser CJ, Adams CA Jr, Eachempati SR (2006) Surgical Infection Society guideline: prophylactic antibiotic use in open fractures: an evidence-based guideline. Surg Infect 7:379–405
15. Saveli CC, Belknap RW, Morgan SJ et al (2011) The role of prophylactic antibiotics in open fractures in an era of community-acquired methicillin-resistant Staphylococcus aureus. Orthopedics 34:611–616
16. Zalavras CG, Patzakis MJ (2003) Open fractures: evaluation and management. J Am Acad Orthop Surg 11:212–219
17. Christy MR, Lipschitz A, Rodriguez E et al (2014) Early postoperative outcomes associated with the anterolateral thigh flap in Gustilo IIIB fractures of the lower extremity. Ann Plast Surg 72: 80–83
18. Bui DT, Cordeiro PG, Hu QY et al (2007) Free flap reexploration: indications, treatment, and outcomes in 1193 free flaps. Plast Reconstr Surg 119:2092–2100
19. Godina M (1986) Early microsurgical reconstruction of complex trauma of the extremities. Plast Reconstr Surg 78(3): 285–292
20. Choudry U, Moran S, Karacor Z (2008) Soft-tissue coverage and outcome of Gustilo grade IIIB midshaft tibia fractures: a 15-year experience. Plast Reconstr Surg 122:479–485
21. Sullivan A, Edlund C, Nord CE (2001) Effect of antimicrobial agents on the ecological balance of human microflora. Lancet Infect Dis 1: 101–114
22. Zalavras CG, Marcus RE, Levin LS, Patzakis M (2007) Management of open fractures and subsequent complications. JBJS [Am] 89-A: 884–895
23. Lee J (1997) Efficacy of cultures in the management of open fractures. Clin Orthop Relat Res 339:71–75