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Two-stage combined ortho-plastic management of type IIIB open diaphyseal tibial fractures requiring flap coverage: Is the timing of debridement and coverage associated with outcomes?

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Conflicts of interest

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1 **Two-stage combined ortho-plastic management of type IIIB open**
2 **diaphyseal tibial fractures requiring flap coverage: Is the timing of**
3 **debridement and coverage associated with outcomes?**

4 **ABSTRACT**

5
6 **Objective:** To delineate whether timing to initial debridement and definitive treatment had an
7 effect on patient outcomes in those undergoing two-stage ortho-plastic management of Gustilo-
8 Anderson type IIIB open tibial diaphyseal fractures.

9 **Design:** Retrospective comparative cohort study over a two year period.

10 **Setting:** Level 1 trauma centre

11 **Patients/Participants:** A total of 148 patients were identified. Following exclusion of ankle
12 fractures, non-diaphyseal fractures and those who did not undergo two-stage ortho-plastic
13 management, 45 patients were eligible for final analysis.

14 **Intervention:** Time to initial debridement and definitive management

15 **Main Outcome Measurement:** Deep infection. Secondary outcomes being nonunion and flap
16 failure. Multiple linear regression was utilised for outcomes. We assumed *a priori* that p values of
17 less than 0.05 were significant.

18 **Results:** Mean age was 54 years (SD 23.0), with 28 males and 17 females. Over a mean 2 year
19 follow up, there were four (4/45) deep infections, two infection associated flap failures and one
20 vascular flap failure. All patients progressed to union. The mean time to initial debridement for
21 the whole cohort was 19 hours (SD 12.3), and the mean time to definitive reconstruction was
22 65 hours (SD 51.7). Longer time to both initial debridement and definitive reconstruction was
23 not found to be significantly associated with deep infection, infected flap failure or nonunion.

24 **Conclusion:** Utilising a two-stage ortho-plastic operative algorithm, timing to initial
25 debridement and definitive fixation with soft tissue coverage was not associated with negative
26 outcomes.

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STUDY TYPE: THERAPEUTIC. LEVEL OF EVIDENCE: III

Introduction

Type IIIB open tibial fractures are severe, high energy injuries that require soft tissue free flap as well as bone reconstruction. Combined orthopaedic and plastic specialist input is key in managing these injuries, and the subsequent emergence of this combined approach is now considered by some to be the gold standard.[1-3] This treatment approach is a core recommendation in the standards of care in the United Kingdom, with the prevention of unfavourable outcomes such as deep infection, nonunion and flap failure being key treatment aims.[4] However, The effect of time to debridement and definitive soft tissue coverage on these outcomes remains contentious. The traditional “six-hour” rule established on the back of evidence by Kindsfater et al.[5] has not stood the test of time and is now considered outdated.[6] Additionally, it is widely accepted that early intervention with combined orthopaedic and plastic surgical input for both the initial debridement and definitive treatment is desirable.[7]

Our unit has utilized a combined ortho-plastic (orthopaedic and plastic surgery) approach for all open fractures, defining a clear staged treatment algorithm for type IIIB open tibial shaft fractures. To validate the safety of the unique approach used in the study unit, timing at every stage is a key component that must be analyzed. We hypothesized that the timing of debridement and definitive coverage may be associated with better outcomes when utilizing a combined ortho-plastic approach consisting of a two-stage debridement and intramedullary nailing for type IIIB open diaphyseal tibial fractures.

53 **Patients & Methods**

54 ***Inclusions and exclusions***

55 This was a retrospective comparative cohort study over a two year period from May 2014 to May
56 2016. A total of 148 consecutive patients were identified that met the BOAST 4 criteria – primarily
57 an open tibial injury which requires transfer to a level 1 trauma centre for specialist care .[4] This
58 comprised 145 type IIIB and 3 type IIIC open tibial fractures. The national Trauma Audit and
59 Research Network (TARN) database was reviewed for these patients along with case notes,
60 operation notes, clinic letters and radiographs. Sixty-one cases were categorized as ankle fractures
61 and were excluded. A further 21 were excluded as they were metaphyseal tibial fractures (9
62 proximal (AO-41) and 12 distal (AO-43)). Seven patients were also excluded due to early mortality
63 pre-operatively (n=1), peri-prosthetic fracture (n=2), primary bone transport procedure (n=2) or
64 primary amputation (n=2). A further 14 patients were not fit for more than one anaesthetic and
65 therefore had initial debridement, definitive fixation and local flap coverage as a single sitting. All
66 type IIIC fractures were excluded as part of the above criteria. A total of 45 patients were therefore
67 eligible for final analysis. This is shown in figure 1.

68

69 ***Surgical interventions***

70 The majority of patients presenting to our (level 1) major trauma centre with an open
71 type IIIB diaphyseal tibial fracture undergo a two-stage ortho-plastic approach.[8] Stage one
72 consists of initial wound excision and thorough debridement, whilst the bone is temporarily
73 stabilized using a 3.5mm LCDCP plate as temporary internal fixation (TIF). External
74 fixation as a temporizing measure has ceased to exist as part of the novel ortho-plastic
75 protocol in the study unit.[9] This has been the case since May 2015, one year prior to the
76 end period of the study. Patients prior to this novel protocol received external fixation. The
77 switch in protocol primarily owed to the unnecessary added risk of pin site infection, which
78 has been shown to be as high as 28%.[10, 11] The use of a temporary internal fixator negates

79 this risk, and can be used (as a bridging device) even in fractures with large zones of
80 comminution, provided there is intact shaft integrity proximal and distal to the plate. This is
81 fixed bicortically following fracture reduction. Use of the plate is a very simple technique
82 that encourages adequate exposure of the zone of injury.[9, 12] All wounds, regardless of
83 type of temporary fixation, were dressed with negative pressure wound therapy (NPWT)
84 and this is not removed until the second stage. Following stage one, the patient is
85 physiologically stabilised until definitive fixation and soft tissue coverage, This is then
86 undertaken on a dedicated ortho-plastics operating list.

87

88 At the second stage, the TIF is removed and the site re-debrided before a fresh transcortical 3.5mm
89 DCP is applied to the anterior tibial cortex. This plate-assisted technique facilitates the
90 intramedullary nailing procedure in all cases as part of the unit's ortho-plastic protocol. Definitive
91 soft tissue free flap coverage and bony stabilisation is then undertaken during this single theatre
92 episode. This second stage has previously been referred to as "fix and flap".[13] Intravenous
93 antibiotics are continued until definitive management has been completed.

94

95 The above treatment algorithm forms the basis for almost all of open tibial fractures treated in our
96 major trauma unit. As per the British Orthopaedic Association Standards for Trauma (BOAST4)
97 [4], we aimed to achieve all initial debridements within 24 hours regardless of whether this was a
98 primary or secondary transfer from another trauma unit. We aimed to achieve the 72 hour target
99 for definitive soft tissue reconstruction.

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104

105 ***Outcomes***

106 The primary outcome measure was deep infection rate with secondary outcomes being nonunion and
107 flap failure.

108

109 The diagnosis of deep infection was based on the criteria for ‘deep incision surgical site infection’,
110 as outlined by the Centers for Disease Control and Prevention (CDC).[14] The primary outcome
111 measure of deep infection was defined as infection requiring surgical debridement and/or prolonged
112 antibiotic therapy following definitive soft tissue reconstruction. The definition was not reliant on
113 positive cultures.

114

115 Diagnosis of nonunion was based on clinical and radiological findings over a minimum clinic
116 follow-up period of >1.2 years, according to the principle outlined by Frölke et al, which reaffirms
117 the contribution of the Weber and Cech model of nonunion, specifying that in long bones, a
118 minimum of 6 months should pass before nonunion is considered.[15, 16] Finally, flap failure was
119 defined as total or partial necrosis of the transferred tissue. Flap failure occurring 1 month or more
120 after definitive coverage was assumed to be secondary to deep infection.

121

122 ***Statistical analysis***

123 Analyses were undertaken with IBM “SPSS” Statistics version 23 (IBM Corp. Released 2015.
124 IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). Descriptive statistics
125 were used for categorical data and Shapiro-Wilkes testing for normality for any continuous data.
126 Parametric data was expressed as mean and standard deviation, with non-parametric data as
127 median and interquartile range (IQR). Collinearity testing via data tolerance and variance inflation
128 factors (VIF) for independent variables was carried out. A data tolerance output of < 0.5 and VIF
129 of > 4 for age and ASA indicated that these two factors were highly correlated. Therefore, ASA
130 was removed from the model. Multiple logistic regression analysis was utilized for the outcomes

131 of deep infection, nonunion and flap failure. The predictor variables analyzed were time to initial
132 debridement, time to definitive fix and flap, whether the patient was a primary referral or secondary
133 transfer, type of temporary fixation (external fixation vs. TIF), flap type, age at the time of injury,
134 gender, laterality, comorbidities (smoking and diabetes), severity of shaft fracture (AO
135 classification) and whether the new plate used to facilitate tibial nailing was retained or removed.
136 Significance for mean time to initial and definitive management was ascertained via an
137 independent samples t-test with the grouping variables being the outcomes described above.
138 Receiver operating characteristic (ROC) curves were used to ascertain timing cut-offs for when a
139 negative outcome would be more likely. We assumed *a priori* that p values of less than 0.05 were
140 significant. The observed power for this study was 0.173 with regards to the primary outcome of
141 deep infection.

142

143 **Results**

144 ***Demographics***

145 A total of 45 patients were included in final analysis, all of whom underwent two-stage
146 definitive bony stabilization and soft tissue coverage as defined in the methods. The mean age
147 of the patients was 54 years (SD 23.0), with 28 males and 17 females. There were 23 left sided
148 injuries with 22 right sided. Eleven patients were smokers at time of injury and 3 were diabetic.
149 The median American Society of Anesthesiologists (ASA) grade was 2 (IQR 1). There was a
150 mean follow up of 2.0 years (SD 0.42). Thirty patients underwent free flap soft tissue
151 reconstruction with 15 undergoing a local flap. Of the free flap group, the majority (25) were
152 anterolateral thigh (ALT) flaps. An external fixator was used in 11 (11/45) patients, with TIF
153 in the remaining 34 (34/45). With regards to fracture severity, 22 (48.9%) shaft fractures were
154 AO type A, 17 (37.8%) type B and 6 (13.3%) type C. The plate was retained in the final
155 construct in 29 patients (64%).

156

157 **Outcomes**

158 A total of 5 (5/45) patients developed complications, with 1 (1/45) metalwork associated infection, 3
159 (3/45) infection associated flap failures and 1 (1/45) vascular associated flap failure.

160

161 For the primary outcome, there were a total of four (4/45) deep infections in this study. This is
162 presented in table 1. Of those who developed deep infection, two were smokers (2/4 in the deep
163 infection group compared to 9/41 in the group that did not develop deep infection; $p=0.499$) and one
164 was diabetic (1/4 in the deep infection group compared to 2/41 in the group that did not develop deep
165 infection; $p=0.077$). There was no association between bone injury severity and the outcomes of deep
166 infection ($p=0.754$), infection or vascular associated flap failures ($p=0.378$, $p=0.997$) and non-union
167 (0.997).

168

169 For secondary outcomes, there were four (4/45) flap failures, three of which (3/4) were associated
170 with infection with one (1/4) a vascular associated flap failure. This vascular associated flap failure
171 was not considered as part of the primary outcome. There were no cases of nonunion.

172

173 **Timing**

174 A total of 17 patients were secondary transfers from a trauma unit within our network, the
175 remainder were direct admissions to our major trauma center. The mean time to initial
176 debridement for the whole cohort was 19 hours (SD 12.3), and the mean time to definitive
177 reconstruction was 65 hours (SD 51.7). Fourteen patients (14/45) were debrided within 12
178 hours, seven of which (7/14) debrided within 6 hours. Thirty-nine (39/45) patients underwent
179 initial debridement within 24 hours, with 32 patients (32/45) undergoing definitive soft tissue
180 reconstruction with fix and flap within 72 hours.

181

182 There was no significant association between secondary transfer from another center and outcomes
183 such as infection (p=0.61, flap failure (p=0.20), and overall complication rate (p=0.29).

184

185 *Timing and outcomes*

186 Of those patients who developed deep infection, the time to initial debridement and definitive
187 reconstruction was comparable to those who did not develop infection. Mean difference in time
188 to initial debridement was under 1 hour when comparing infected and non-infected groups
189 (p=0.990). This was also under 1 hour for time to definitive management (p=0.952). Patients
190 who were transferred had a longer mean time to initial debridement, with a mean difference of
191 10 hours (p=0.01) (Table 2).

192

193 For those who developed infection associated flap failure, time to initial debridement was lower
194 (mean difference 3 hours), compared to those who did not develop this. However mean time to
195 definitive treatment was longer (mean difference 9 hours) than those who did not develop this
196 complication. The differences were not significant (p=0.724, p=0.873 respectively)).

197

198 There was one case of ALT flap failure alone, which was as a result of a microvascular event and
199 happened at less than 24 hours after the second stage reconstruction. This was associated with a
200 significant increase in time to initial debridement (p = 0.007). These figures are represented in
201 Table 3.

202

203 For the significant results above, no time-point seemed to offer a definitive cut-off to determine
204 optimal timing for initial and definitive debridement that would lead to a reduced odds of
205 associated negative outcomes.

206

207 Independent variables including age, gender, laterality, type of flap, type of temporary fixation and
208 whether the fresh plate was retained as part of final fixation construct (following nailing) were not
209 found to be predictive of the primary or secondary outcomes.

210

211 **Discussion**

212 This study analyzes both time to initial and definitive bone and soft tissue management in the
213 context of a two-stage ortho-plastic technique for open type IIIB tibial shaft fractures. We report
214 low infection (8.9%), flap failure (8.9%) and no nonunions with use of a coordinated ortho-plastic
215 treatment protocol for type IIIB open tibial fractures. Whilst underpowered, the data demonstrates
216 no association between an increased time to management and the primary outcome of deep
217 infection. Furthermore, there was no significant association between secondary transfer from
218 another center and the development of a deep infection.

219

220 To the authors' best knowledge, there is limited evidence on the use of a two-stage ortho-plastic
221 approach in the management of type IIIB open tibial fractures, particularly with regards to timing.
222 Traditional management of this type of injury involves skeletal stabilization using an external
223 fixator following first debridement. This is usually followed by definitive stabilization and soft
224 tissue coverage, often performed at two separate surgical sittings.[10, 17] This study follows a
225 novel protocol and treatment algorithm that consists of initial aggressive debridement and
226 temporary internal fixation in the majority (34/45, 75.6%) of cases. This is followed by definitive
227 management at a later date with definitive bony stabilization and soft tissue coverage performed
228 as a single procedure. The benefits of a definitive ortho-plastic reconstruction as a combined
229 procedure on deep infection has previously been reported by Mathews et al.[8] In their study, the
230 deep infection rate was found to be significantly reduced under this protocol (4.2%) compared to
231 those who had fixation and soft tissue coverage over two separate theatre visits (34.6%). Since the
232 publication of this paper, our unit has adopted this protocol as standard.

233 The deep infection rate in this study is 8.9% and this compares favorably to other studies.[8, 12,
234 18-22] Certain factors are known to reduce complication rates in these injuries including antibiotic
235 prophylaxis [23] and early transfer to a major trauma center with combined orthopaedic and plastic
236 surgical input.[24] More recently, the LEAP group looked at timing in the management of 315
237 patients with varying degrees of open lower limb and ankle fractures. Time from injury to initial
238 debridement was not found to be a predictor of deep infection, however timely transfer to an
239 appropriate treating center was.[25] An even larger multi-center prospective study by Weber et al
240 has also analyzed timing of surgery in relation to outcomes. In 736 patients looking at all open
241 injuries, factors associated with an increased risk of infection were increasing Gustilo type or tibial
242 injuries. Time to surgery did not seem to be associated with the risk of infection, although in their
243 study the deep infection rate of type IIIB tibial fractures was 18%, with the overall complication
244 rate of type IIIB injuries including upper limb being 16%.[24] Other significant studies have also
245 failed to establish an association between timing of debridement and negative outcomes,
246 particularly infection. Patzakis et al. showed there was a marginally increased infection rate in
247 open fracture in those with a time to debridement over 12 hours, but this finding was not
248 statistically significant.[26] This is supported by others in the literature.[27, 28] Perhaps the most
249 robust study to contradict a negative correlation with timing was that by Hull et al, which
250 consecutively analyzed 364 patients with 459 open injuries. In this series of all upper and lower
251 limb open fractures presenting to their unit, every one hour delay to debridement was associated
252 with a 3.3% increase in deep infection rate, with a greater absolute effect on type IIIB/C tibial
253 injuries. It was also suggested that timing of definitive procedure, type of anesthetic used and tibial
254 site were all additive factors in determining infection rate.[29] The authors also postulate that since
255 2010, and with the emergence of LEAP data, the creation of the major trauma network in the UK
256 has been successful in reducing delay in patient transfer and time from injury to debridement. This
257 has contributed to the similar timings seen in our study for both initial and definitive debridement
258 regardless of whether the patient was a primary referral or secondary transfer.

259 In this study, there was no association between bony severity and nonunion, with no patients
260 developing this complication. This may be attributed to a lower proportion (13.3%) of patients
261 sustaining an AO type C bony injury, in comparison to literature where nonunion rates vary from
262 41-60% in those with severe injury and bone loss.[17, 30, 31]

263

264 In our study one patient experienced non-infective ALT flap failure attributed to a microvascular
265 event. This 82 year old diabetic patient underwent a significantly longer time to initial debridement
266 (initial debridement 86 hours, final reconstruction 217 hours). The failed flap was revised to a local
267 flap and split skin grafting with no further complications. In addition to risk factors such as age
268 [32-35] and diabetes [36-38], delayed flap reconstruction is a recognized risk factor for flap failure.
269 The mechanism by which early flap coverage is thought to be important revolves around the
270 obliteration of dead space by a healthy conforming muscle flap.[13] This is designed to reduce
271 bacterial contamination and subsequent local inflammatory response, with avoidance of pro-
272 thrombotic and fibrotic effects that lead to flap failure.[39] In addition, it is believed that bringing
273 healthy muscle into clean fracture site introduces vital humoral and cellular elements which are
274 critical to the fracture healing process.[40] Infection rates seem to be lower as there are studies
275 that indicate delay of flap coverage converts any contaminated wounds into colonized wounds.[41,
276 42]

277

278 In this respect, Godina was a strong proponent of microvascular reconstruction within 72 hours of
279 open injury. Along with faster bony union, flap failure and infection rates were lower in the early
280 compared to delayed flap coverage group.[43] This is further supported by Hertel et al [44] and
281 Gopal et al [13, 40] both of whom conducted studies showing similar outcomes of lower infection
282 rate and faster bony union in those undergoing flap coverage within 72 hours. Furthermore, Wood
283 et al conducted a systematic review of literature in 2012, comparing early, intermediate and late
284 flap coverage in open fractures. He concluded that whilst the optimal timing of flap coverage

285 remains controversial, a delay in flap coverage in open fractures leads to an increased likelihood
286 of negative bony and soft tissue outcomes.

287

288 There are key strengths to this study, namely that this is a study looking at timing in this novel
289 approach to the management of type IIIB open tibial fractures. Furthermore, in our department,
290 we are afforded the opportunity to assess both orthopaedic and plastic surgical outcomes in
291 tandem, allowing a more complete analysis of these patients. This study represents a consecutive
292 cohort of patients with similar injuries and management strategy. There are limitations to our study
293 design, this was a retrospective study offering an inferior level of evidence compared to a
294 prospective study. The retrieval of past data allows for recall bias. Furthermore, any significant
295 data in this study will show an association but not necessarily causation. This is particularly in
296 view of the low post-hoc power of this study meaning that whilst the authors are confident of their
297 findings based on accurate data and analysis, conclusions should be made with relative caution.
298 This is particularly relevant as one case of vascular associated flap failure led to a skew of results,
299 highlighting the need for greater patient numbers to make a firm conclusion. None of our patients
300 proceeded to nonunion however a future study could include further information such as delayed
301 union or functional scores.

302

303 ***Conclusion***

304 Utilizing a two-stage approach with combined ortho-plastic reconstruction is associated with
305 favorable outcomes in comparison to the published literature. The timing of intervention does not
306 appear critical in determining the risk of adverse outcomes. However, early operative management
307 of open tibial fractures is advocated in a safe and timely manner within a definitive ortho-plastic
308 center.

309

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TABLE AND FIGURE LEGENDS

Table 1. Details of deep infection management per patient.

Table 2. Time to initial management based on transfer or direct admission.

Table 3. Timing and associated complications

Figure 1. Flowchart of inclusions and exclusions.

Table 1. Details of deep infection management per patient.

	Type	Diagnosis	Time point	Cultures	Operation
Patient 1	Infected metalwork	Deep tissue samples	12 months post-operatively	B-haemolytic streptococcus	Removal of metalwork
Patient 2	Infection associated flap failure	Deep tissue samples	10 weeks post-operatively	Staphylococcus Aureus	Staged revision fixation and flap using circular frame
Patient 3	Infection associated flap failure	Deep tissue samples	2 weeks post-operatively	Enterobacter Cloacae	Exchange tibial nailing
Patient 4	Infection associated flap failure	<ol style="list-style-type: none"> 1. Clinical assessment (rising CRP and new pain) 2. Deep tissue samples 	16 weeks post-operatively	Culture negative (commenced on empirical antibiotics)	Exchange tibial nailing

Table 2. Time to initial management based on transfer or direct admission.

Transfer	Number	Mean hours to initial debridement	Standard Deviation	Significance (p<0.05)
Yes	17	25.2	16.9	Yes
No	28	15.10	6.4	

Table 3. Timing and associated complications

		Number	Mean hours to initial debridement	Mean hours to definitive treatment
Infection	Yes	4	18.9 (SD 7.68)	66.0 (SD 20.4)
	No	41	18.9 (SD 12.8)	67.9 (SD 62.7)
Infection associated flap failure	Yes	3	15.8 (SD 8.01)	74.5 (SD 26.6)
	No	42	19.0 (SD 12.6)	67.4 (SD 61.3)
Flap failure	Yes	1	86.15 (p<0.001)	217.7 (p=0.01)
	No	44	17.4 (SD 6.97)	64.4 (SD 56.2)

