

Higher Reoperation Rates in Planned, Staged Treatment of Open Fractures Compared with Fix-and-Close

A Propensity Score-Matched Analysis

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Background: Initial surgical management of Gustilo-Anderson type-I to IIIA open fractures varies from surgical fixation of the fracture with immediate closure of the traumatic wound to various combinations of staged fracture and wound management. The decision to choose staged management has historically been based on wound contamination and the severity of the open fracture. The purpose of this study was to compare the rates of surgical site infection (SSI), wound complication, nonunion, and 1-year reoperation between patients with type-I to IIIA open fractures who underwent fix-and-close treatment and those who underwent planned, staged treatment.

Methods: This is a secondary analysis of participants who were enrolled in the Aqueous-PREP and PREPARE-Open studies, excluding those with type-IIIB and IIIC open fractures. Participants were divided into fix-and-close or planned, staged groups and were matched using propensity scores that were computed with multiple variables, including patient and injury characteristics. Associations between treatment type and outcomes were analyzed.

Results: A total of 3,170 participants (staged, 872: 70% White, 20% Black, and 10% other or unknown race; fix-and-close, 2,298: 62% White, 21% Black, and 17% other) with Gustilo-Anderson type-I to IIIA open fractures were identified. Eight hundred and thirty-six participants who underwent planned, staged treatment were propensity score-matched to 836 participants who underwent fix-and-close treatment. Staged treatment was significantly associated with increased odds of deep SSI within 90 days (odds ratio [OR], 2.0 [95% confidence interval (CI), 1.15 to 3.47]; $p = 0.01$) and reoperation specifically for infection within 1 year (OR, 1.47 [95% CI, 1.06 to 2.04]; $p = 0.02$) but was not associated with increased odds of wound dehiscence (OR, 0.85 [95% CI, 0.49 to 1.49]; $p = 0.57$), wound necrosis or failure of the wound to heal (OR, 1.37 [95% CI, 0.83 to 2.25]; $p = 0.21$), reoperation requiring any free or local flap coverage (OR, 0.96 [95% CI, 0.55 to 1.68]; $p = 0.89$), or reoperation for delayed union or nonunion (OR, 1.30 [95% CI, 0.92 to 1.83]; $p = 0.14$).

Conclusions: Fix-and-close treatment of open fractures of type IIIA and lower was associated with decreased odds of deep SSI within 90 days and reoperation for infection within 1 year without an increased risk of wound complications or nonunion and may be considered even in fractures with embedded contamination provided that adequate debridement is performed.

Level of Evidence: Therapeutic Level II. See Instructions for Authors for a complete description of levels of evidence.

*Members of the PREP-IT Investigators are included as a note at the end of the article.

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Open fractures carry an inherent risk of developing surgical site infections (SSIs) and wound-healing complications due to the injury disrupting soft tissue and exposing both bone and soft tissue to contamination. Despite the treatment of open fractures having been studied extensively, resulting in a substantial body of evidence regarding the early administration of antibiotics, meticulous debridement, the type and method of irrigation, and the timing of soft-tissue coverage in type-IIIB open fractures, the timing of wound closure in type-IIIA open fractures or lower-type open fractures remains controversial. Historically, a second debridement with delayed wound closure was advocated to allow drainage to prevent the collection of contaminated tissue and fluid. This treatment strategy has been traced back to World Wars I and II during the pre-antibiotic era¹⁻³. Currently, the timing of fracture fixation is often planned on the basis of wound closure in order to avoid exposing metal work to the environment while waiting for definitive wound closure^{4,5}. Advancements in surgical technique and the introduction of antibiotics have challenged this practice. Indeed, it has been demonstrated that primary wound closure is safe in non-contaminated wounds⁶⁻⁹. However, there are no clear guidelines regarding the timing of wound closure in open fractures with contamination, and the decision is largely left to the judgement and experience of the treating surgeon.

The purpose of this study was to compare the rates of SSI, wound complication, nonunion, and 1-year reoperation between patients with type-I to IIIA open fractures, with or without contamination, who underwent fix-and-close treatment versus planned, staged treatment. The hypothesis of the study was that fix-and-close treatment would not lead to higher rates of the measured outcomes.

Materials and Methods

A Program of Randomized Trials to Evaluate Preoperative Antiseptic Skin Solutions in Orthopaedic Trauma (PREP-IT) consisted of 2 trials. These were A Pragmatic Randomized Trial Evaluating Preoperative Aqueous Antiseptic Skin Solutions in Open Fractures (Aqueous-PREP), which compared 10% povidone-iodine versus 4% chlorhexidine gluconate in aqueous solutions, and A Pragmatic Randomized Trial Evaluating Preoperative Alcohol Skin Solutions in Fractured Extremities (PREPARE), which compared 3M DuraPrep (iodine-povacrylex [0.7% free iodine]) versus BD (Becton Dickinson) ChlorPrep (2% chlorhexidine gluconate) in alcohol solutions. The present study is a secondary analysis of participants who were enrolled in the Aqueous-PREP and PREPARE-open studies^{10,11}. Participants with Gustilo-Anderson type-IIIB and IIIC open fractures were excluded from this analysis. Ethical approval for this analysis was obtained from the Hamilton Integrated Research Ethics Board (HiREB #17591).

Participants were divided into 2 groups on the basis of whether fix-and-close or planned, staged treatment strategies were utilized. These groups were then matched using propensity scores that were computed with multiple variables, including age, gender, body mass index, educational attain-

ment, medical insurance, Functional Comorbidity Index, renal disease, diabetes, HIV (human immunodeficiency virus), smoking status, Gustilo-Anderson classification, embedded wound contamination and bone loss based on the Orthopaedic Trauma Association Open Fracture Classification (OTA-OFC)¹², local antibiotic use, injury mechanism, fracture anatomic location¹³ (humerus: OTA/AO 11, 12, and 13; radius and ulna: OTA/AO 21, 22, and 23; femur: OTA/AO 31 to 34; tibia: OTA/AO 41 to 44; pelvis: OTA/AO 61 and 62; hand: OTA/AO 71 to 79; foot: OTA/AO 81 to 89), workplace injury, American Society of Anesthesiologists (ASA) physical status, and Injury Severity Score (ISS). The optimal propensity score-matching method was used to minimize covariate imbalance between the participants in the fix-and-close group and those in the staged treatment group; additionally, highly influential variables, including embedded wound contamination, bone loss, and Gustilo-Anderson classification, were exactly matched to ensure complete comparability between the groups.

Propensity score matching was performed with use of the MatchIt package (R statistical software; R Foundation for Statistical Computing). To assess the balance of covariates after matching, the absolute standardized mean difference (SMD) was utilized because it emphasizes differences in proportions and, unlike the p value, is not dependent on sample size¹⁴. Variables with an SMD of <0.1 were considered optimally balanced. Propensity score values for each treatment group before and after matching were plotted in histograms.

The clinical outcomes of interest were any SSI; deep SSI; and any unplanned reoperation for wound dehiscence, wound necrosis or failure of the wound to heal, a free or local flap, or delayed union or nonunion. Associations between treatment type and each outcome were analyzed with use of logistic regression for the full dataset of study participants and with use of conditional logistic regression for the matched subset. The threshold for statistical significance was set at $p < 0.05$. Additionally, the relationship between treatment type and an ordinal outcome indicating each participant's most severe wound-complication event—categorized in descending severity as free or local flap, skin graft, revision wound closure, or no reoperation—were analyzed with use of proportional odds models. Lastly, external and internal fixation methods, stratified by fracture location, were examined for associations with the outcomes of interest in each of the treatment groups. SSI was defined according to the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network criteria¹⁵. SSI included superficial incisional infection within 30 days after fracture surgery, deep incisional or organ-space infection within 90 days after fracture surgery, and any SSI that met the CDC definition within 12 months after surgery. Reoperation events included any unplanned return to the operating theater for infection, wound-healing complications, or fracture-healing complications. Of note, planned, staged reoperations, such as staged bone grafting or skin grafting, were not counted as reoperation events.

TABLE I Patient Characteristics of the Overall Study Population and Propensity Score-Matched Subset*

Characteristic	Overall (N = 3,170)			Propensity Score-Matched† (N = 1,672)		
	Staged (N = 872)	Fix-and-Close (N = 2,298)	P Value‡	Staged (N = 836)	Fix-and-Close (N = 836)	P Value‡
Age (yr)	43 (30, 57)	42 (29, 59)	0.49	43 (30, 57)	42 (29, 58)	0.41
Gender			0.59			0.31
Female	339 (39%)	869 (38%)		326 (39%)	305 (36%)	
Male	533 (61%)	1,427 (62%)		510 (61%)	531 (64%)	
Not reported	0 (0%)	2 (0.1%)		0 (0%)	0 (0%)	
Race§			<0.001			0.005
White	609 (70%)	1,421 (62%)		583 (70%)	530 (63%)	
Black	174 (20%)	481 (21%)		167 (20%)	174 (21%)	
Asian	8 (0.9%)	26 (1.1%)		8 (1.0%)	7 (0.8%)	
American Indian or Alaska Native	10 (1.1%)	16 (0.7%)		10 (1.2%)	7 (0.8%)	
Native Hawaiian or Other Pacific Islander	1 (0.1%)	2 (0.1%)		1 (0.1%)	1 (0.1%)	
Other racial group	12 (1.4%)	28 (1.2%)		11 (1.3%)	13 (1.6%)	
Prefer not to answer	10 (1.1%)	21 (0.9%)		10 (1.2%)	10 (1.2%)	
Missing data	48 (5.5%)	303 (13%)		46 (5.5%)	94 (11%)	
Hispanic ethnicity§	105 (12%)	207 (9.0%)	0.01	102 (12%)	81 (9.7%)	0.10
Education			<0.001			0.23
High school diploma or less	417 (48%)	1,034 (45%)		404 (48%)	397 (47%)	
Some college or associate's degree	244 (28%)	555 (24%)		234 (28%)	222 (27%)	
Bachelor's degree	108 (12%)	348 (15%)		100 (12%)	118 (14%)	
Graduate degree	59 (6.8%)	154 (6.7%)		56 (6.7%)	43 (5.1%)	
Prefer not to answer	44 (5.0%)	207 (9.0%)		42 (5.0%)	56 (6.7%)	
Medical insurance	668 (77%)	1,909 (83%)	<0.001	640 (77%)	642 (77%)	0.95
Body mass index classification			<0.001			0.86
Underweight	8 (0.9%)	35 (1.5%)		8 (1.0%)	8 (1.0%)	
Healthy weight	202 (23%)	681 (30%)		197 (24%)	189 (23%)	
Overweight	262 (30%)	770 (34%)		244 (29%)	260 (31%)	
Obese	400 (46%)	812 (35%)		387 (46%)	379 (45%)	
Current smoking	289 (33%)	789 (34%)	0.55	278 (33%)	261 (31%)	0.40
Functional Comorbidity Index (points)	1 (0, 2)	1 (0, 2)	<0.001	1 (0, 2)	1 (0, 2)	0.48
Renal disease	4 (0.5%)	25 (1.1%)	0.15	4 (0.5%)	5 (0.6%)	>0.99
Diabetes	88 (10%)	218 (9.5%)	0.65	83 (9.9%)	97 (12%)	0.31
HIV	1 (0.1%)	12 (0.5%)	0.20	1 (0.1%)	2 (0.2%)	>0.99
Gustilo-Anderson classification			<0.001			0.70
Type I	99 (11%)	692 (30%)		99 (12%)	89 (11%)	
Type II	267 (31%)	826 (36%)		264 (32%)	274 (33%)	
Type IIIA	506 (58%)	780 (34%)		473 (57%)	473 (57%)	
OTA-OFC: embedded wound contamination	124 (14%)	114 (5.0%)	<0.001	97 (12%)	97 (12%)	>0.99
OTA-OFC: bone loss			<0.001			>0.99
None	482 (55%)	1,602 (70%)		474 (57%)	474 (57%)	
Bone missing or devascularized bone fragments	337 (39%)	658 (29%)		332 (40%)	332 (40%)	
Segmental bone loss	53 (6.1%)	38 (1.7%)		30 (3.6%)	30 (3.6%)	
Injury mechanism			<0.001			0.19
Motor vehicle	543 (62%)	1,161 (51%)		516 (62%)	505 (60%)	

continued

TABLE I (continued)

Characteristic	Overall (N = 3,170)			Propensity Score-Matched† (N = 1,672)		
	Staged (N = 872)	Fix-and-Close (N = 2,298)	P Value‡	Staged (N = 836)	Fix-and-Close (N = 836)	P Value‡
Fall	219 (25%)	663 (29%)		217 (26%)	203 (24%)	
Other	110 (13%)	474 (21%)		103 (12%)	128 (15%)	
Fracture location#			<0.001			0.88
Humerus	50 (5.7%)	178 (7.7%)		47 (5.6%)	47 (5.6%)	
Radius/ulna	109 (13%)	465 (20%)		106 (13%)	90 (11%)	
Femur	134 (15%)	406 (18%)		125 (15%)	131 (16%)	
Tibia	483 (55%)	1,090 (47%)		467 (56%)	479 (57%)	
Pelvis	14 (1.6%)	15 (0.7%)		13 (1.6%)	9 (1.1%)	
Hand	6 (0.7%)	21 (0.9%)		6 (0.7%)	6 (0.7%)	
Foot	76 (8.7%)	123 (5.4%)		72 (8.6%)	74 (8.9%)	
Any local antibiotic use	76 (8.7%)	288 (12.5%)	0.003	75 (9.0%)	87 (10.4%)	0.84
Local antibiotic type**			0.03			0.31
Vancomycin only	61 (80%)	258 (90%)		60 (80%)	76 (87%)	
Vancomycin and tobramycin	14 (18%)	28 (9.7%)		14 (19%)	11 (13%)	
Vancomycin and other antibiotic	0 (0.0%)	2 (0.7%)		0 (0.0%)	0 (0.0%)	
Tobramycin only	1 (1.3%)	0 (0.0%)		1 (1.3%)	0 (0.0%)	
Workplace injury	91 (10%)	215 (9.4%)	0.39	87 (10%)	85 (10%)	0.94
ASA physical status			<0.001			0.39
1	69 (7.9%)	245 (11%)		66 (7.9%)	75 (9.0%)	
2	346 (40%)	1,033 (45%)		334 (40%)	349 (42%)	
3	352 (40%)	837 (36%)		339 (41%)	325 (39%)	
4	88 (10%)	178 (7.7%)		85 (10%)	82 (9.8%)	
5	17 (1.9%)	5 (0.2%)		12 (1.4%)	5 (0.6%)	
ISS (points)	10 (9, 19)	10 (9, 14)	<0.001	10 (9, 18)	10 (9, 18)	0.27

*Values are given as the median, with the interquartile range in parentheses, or as the number of patients, with the percentage in parentheses. HIV = human immunodeficiency virus; OTA-OFC = Orthopaedic Trauma Association Open Fracture Classification, ASA = American Society of Anesthesiologists, ISS = Injury Severity Score. †Propensity score covariates included age, gender, body mass index, Functional Comorbidity Index, renal disease, diabetes, HIV, current smoking, injury mechanism, fracture location, workplace injury, ASA physical status, ISS, OTA-OFC: embedded wound contamination (exact match), OTA-OFC: bone loss (exact match), and Gustilo-Anderson classification (exact match; I/II versus IIIA). ‡The Wilcoxon rank-sum test was used for continuous data, and the Pearson chi-square test was used for categorical data. §Race and ethnicity were self-reported. #Humerus: OTA/AO 11, 12, and 13. Radius and ulna: OTA/AO 21, 22, and 23. Femur: OTA/AO 31 to 34. Tibia: OTA/AO 41 to 44. Pelvis: OTA/AO 61 and 62. Hand: OTA/AO 71 to 79. Foot: OTA/AO 81 to 89. **Percentages are based on the total number of participants with any local antibiotic use in that group.

Results

A total of 3,170 participants with type-I to IIIA open fractures were identified. Participant characteristics are detailed in Table I. Staged treatment was performed in 872 participants, and fix-and-close treatment was performed in 2,298 participants. In this sample, 1,573 participants had an open fracture of the tibia and 1,597 participants had non-tibial open fractures. A total of 238 participants presented with open fractures with embedded wound contamination. Before propensity score matching, 124 (14%) of the participants in the staged treatment group had embedded wound contamination compared with 114 (5%) of the participants in the fix-and-close group ($p < 0.001$). Supplemental Table I shows the number of participants with a given number of planned surgeries (see Appendix). The number of participants

with embedded contamination increased with the severity of the open fracture based on the Gustilo-Anderson classification ($p < 0.001$; see Appendix Supplemental Table II).

A total of 836 participants from the planned, staged treatment group were propensity score-matched to a total of 836 participants from the fix-and-close group (Table I). The variables used in the propensity score calculation were well balanced between the 2 treatment groups (see Appendix Supplemental Fig. 1), including the Gustilo-Anderson classification (staged group: type I, $n = 99$; type II, $n = 264$; type IIIA, $n = 473$; fix-and-close group: type I, $n = 89$; type II, $n = 274$; type IIIA, $n = 473$; $p = 0.70$), embedded wound contamination ($n = 97$ in each group; $p > 0.99$), and the severity of bone loss (staged group: none, $n = 474$; bone missing or devascularized

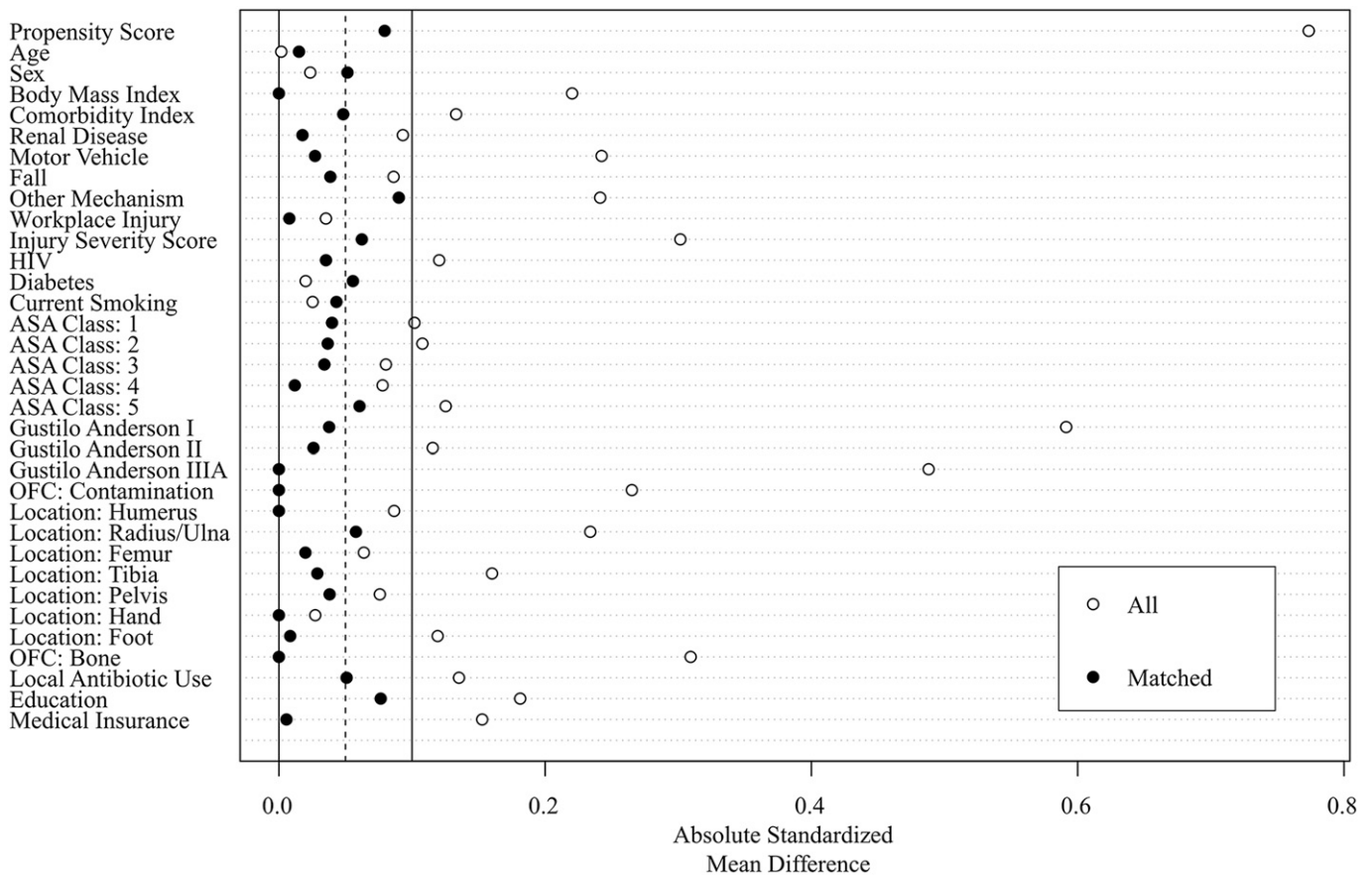


Fig. 1
Standardized mean differences (SMDs) in the overall study population and matched subset. After matching, all covariates demonstrated improved balance, with SMDs of <0.1 (rightmost solid black line) indicating an acceptable level of covariate similarity between the treatment groups. The dashed line represents an SMD of 0.05. Anatomic fracture locations consisted of the humerus (OTA/AO 11, 12, and 13), radius and ulna (OTA/AO 21, 22, and 23), femur (OTA/AO 31 to 34), tibia (OTA/AO 41 to 44), pelvis (OTA/AO 61 and 62), hand (OTA/AO 71 to 79), and foot (OTA/AO 81 to 89). ASA = American Society of Anesthesiologists, OFC = Open Fracture Classification.

bone fragments, $n = 332$; segmental bone loss, $n = 30$; fix-and-close group: none, $n = 474$; bone missing or devascularized bone fragment, $n = 332$; segmental bone loss, $n = 30$; $p > 0.99$). Figure 1 shows the SMDs in the overall study population and in the matched subset. After propensity score matching, all SMDs were <0.1, indicating an acceptable level of covariate similarity between the treatment groups¹⁴.

Table II shows the results of the analyses of various outcomes in the entire participant population and in the propensity score-matched subset. In the entire population, staged treatment was significantly associated with increased odds of any SSI within 90 days (odds ratio [OR], 1.82 [95% confidence interval (CI), 1.35 to 2.45]; $p = 0.0001$), deep SSI within 90 days (OR, 2.79 [95% CI, 1.81 to 4.28]; $p < 0.0001$), any SSI within 1 year (OR, 2.06 [95% CI, 1.61 to 2.63]; $p < 0.0001$), any unplanned reoperation within 1 year (OR, 2.19 [95% CI, 1.77 to 2.71]; $p < 0.0001$), reoperation for infection within 1 year (OR, 2.39 [95% CI, 1.82 to 3.13]; $p < 0.0001$), wound necrosis or failure of the wound to heal (OR, 2.16 [95% CI, 1.43 to 3.24]; $p = 0.0002$), any free or local flap (OR, 1.96 [95% CI,

1.21 to 3.15]; $p = 0.005$), and reoperation for delayed union or nonunion (OR, 2.01 [95% CI, 1.51 to 2.68]; $p < 0.0001$). There was no association between staged treatment and wound dehiscence (OR, 1.60 [95% CI, 0.98 to 2.58]; $p = 0.06$). After propensity score matching, all significant associations were attenuated; however, staged treatment remained significantly associated with increased odds of deep SSI within 90 days (OR, 2.0 [95% CI, 1.15 to 3.47]; $p = 0.01$) and reoperation for infection within 1 year (OR, 1.47 [95% CI, 1.06 to 2.04]; $p = 0.02$).

When looking specifically at wound-related outcomes (Table III) in the full participant population, individuals in the staged treatment group had higher odds of experiencing a higher-severity outcome than individuals in the fix-and-close group (OR, 2.48 [95% CI, 1.74 to 3.52]). However, staged treatment was not significantly associated with this ordinal outcome variable in the matched subset (OR, 1.28 [95% CI, 0.87 to 1.89]).

Supplemental Tables 3 and 4 show the results of the unadjusted analyses for open tibial fractures, non-tibial open fractures, and fractures stratified by Gustilo-Anderson classification (see Appendix). Deep SSI within 90 days, any SSI

TABLE II Associations Between Staged Treatment and Outcomes in the Full Dataset and Propensity Score-Matched Subset*

Outcome	Full Dataset, Unadjusted† (N = 3,170)				Propensity Score-Matched‡ (N = 1,672)			
	Staged (N = 872)	Fix-and-Close (N = 2,298)	OR (95% CI)	P Value	Staged (N = 836)	Fix-and-Close (N = 836)	OR (95% CI)	P Value
Any SSI within 90 days	77 (8.8%)	116 (5.0%)	1.82 (1.35-2.45)	0.0001	70 (8.6%)	62 (7.4%)	1.15 (0.80-1.65)	0.46
Deep SSI within 90 days	44 (5.0%)	43 (1.9%)	2.79 (1.81-4.28)	<0.0001	40 (4.8%)	21 (2.5%)	2.0 (1.15-3.47)	0.01
Any SSI within 1 year	126 (14.4%)	174 (7.6%)	2.06 (1.61-2.63)	<0.0001	116 (13.9%)	93 (11.1%)	1.29 (0.96-1.72)	0.09
Any unplanned reoperation within 1 year	174 (20.0%)	235 (10.2%)	2.19 (1.77-2.71)	<0.0001	156 (18.7%)	125 (15.0%)	1.30 (1.00-1.67)	0.05
Reoperation for infection within 1 year	107 (12.3%)	127 (5.5%)	2.39 (1.82-3.13)	<0.0001	99 (11.8%)	71 (8.5%)	1.47 (1.06-2.04)	0.02
Wound dehiscence	27 (3.1%)	45 (2.0%)	1.60 (0.98-2.58)	0.06	26 (3.1%)	30 (3.6%)	0.85 (0.49-1.49)	0.57
Wound necrosis or failure of the wound to heal	43 (4.9%)	54 (2.3%)	2.16 (1.43-3.24)	0.0002	38 (4.5%)	28 (3.3%)	1.37 (0.83-2.25)	0.21
Any free or local flap	30 (3.4%)	41 (1.8%)	1.96 (1.21-3.15)	0.005	25 (3.0%)	26 (3.1%)	0.96 (0.55-1.68)	0.89
Reoperation for delayed union or nonunion	87 (10.0%)	120 (5.2%)	2.01 (1.51-2.68)	<0.0001	77 (9.2%)	60 (7.2%)	1.30 (0.92-1.83)	0.14

*Values are given as the number of patients, with the percentage in parentheses. †Logistic regression. ‡Conditional logistic regression.

within 1 year, any unplanned reoperation within 1 year, and reoperation for infection within 1 year remained associated with staged treatment in open tibial fractures, non-tibial open fractures, and Gustilo-Anderson type-IIIA fractures. Any SSI within 1 year, unplanned reoperation within 1 year, and reoperation for infection within 1 year were associated with staged treatment in Gustilo-Anderson type-II open fractures, whereas no outcomes were associated with staged treatment in Gustilo-Anderson type-I open fractures.

Supplemental Table V shows data on the relationship between fixation method and treatment type for each fracture location, and Supplemental Table VI shows the association between the fixation method and outcomes in the subgroup of patients with tibial fractures (see Appendix). The internal fixation method utilized for femoral and tibial fractures significantly differed between the treatment groups in the entire population (femur, $p = 0.026$; tibia, $p < 0.001$)

and in the propensity score-matched subset ($p = 0.021$ and $p < 0.001$, respectively), with plate(s)/screw fixation being more common in the staged treatment group and intramedullary nail fixation being more common in the fix-and-close group. In the tibial fracture subgroup after matching, use of both an intramedullary nail and plate(s) and screws was significantly associated with an unplanned local or free flap.

In sensitivity analyses that accounted for clustering by trauma center using mixed-effects logistic regression and that excluded patients who had ≥ 3 planned surgeries (i.e., compared fix-and-close to only 1 additional debridement), staged treatment was significantly associated with increased odds of deep SSI within 90 days, any SSI within 1 year, any unplanned reoperation within 1 year, and reoperation for infection within 1 year (see Appendix Supplemental Table VII).

TABLE III Association Between Staged Treatment and Increasingly Severe Outcomes in the Full Dataset and Propensity Score-Matched Subset*

Outcome, by increasing severity	Overall (N = 3,170)			Propensity Score-Matched (N = 1,672)		
	Staged (N = 872)	Fix-and-Close (N = 2,298)	P Value†	Staged (N = 836)	Fix-and-Close (N = 836)	P Value†
None of these events	812 (93.1%)	2,233 (97.2%)	<0.0001	785 (93.9%)	796 (95.2%)	0.29
Revision wound closure	14 (1.6%)	15 (0.7%)		14 (1.7%)	8 (1.0%)	
Skin graft	16 (1.8%)	9 (0.4%)		12 (1.4%)	6 (0.7%)	
Free or local flap	30 (3.4%)	41 (1.8%)		25 (3.0%)	26 (3.1%)	

*Values are given as the number of patients, with the percentage in parentheses. †Pearson chi-square test.

Discussion

In this secondary analysis of the Aqueous-PREP and PREPARE-Open studies, we found in both the unadjusted and propensity score-matched analyses that patients with open fractures of type IIIA or lower who underwent planned, staged treatment had higher rates of deep SSI within 90 days and reoperation for infection within 1 year than those who underwent fix-and-close treatment. The propensity score analyses exactly matched for Gustilo-Anderson classification, OTA-OFC embedded wound contamination, and OTA-OFC bone loss. These results suggest that, if an open fracture of type IIIA or lower is sufficiently debrided, it should be fixed and closed without a planned second look. This treatment paradigm appears to be no worse than a planned, staged approach, and our data suggest that it is likely better at decreasing SSIs.

A high rate of deep infection in the setting of primary wound closure (20%) compared with delayed closure (3%) was reported by Russell et al.¹⁶ in a study of 90 type-IIIA or lower open tibial fractures in 1990. The results from more recent studies have favored primary wound closure, with deep infection rates of 5% in primary closure versus 9% to 18% in delayed closure^{8,9,17}. Although the overall infection rate in the present study is slightly higher than these previously reported infection rates, primary closure of the wound was associated with a significant decrease in deep SSIs and reoperations for infection. The swinging of the pendulum from delayed wound closure to primary closure in open fractures can potentially be explained by the standardization of antibiotic administration and improvements in surgical technique. Historically, contamination of the wound may have precluded primary closure in open fractures. The management of open fractures has evolved to include systemic and local antibiotic use, changes in the timing of irrigation and debridement, and multidisciplinary and multimodal soft-tissue management. Compared with the historical practice of planned second-look debridements, a fix-and-close strategy may now be plausible because of this evolution in open fracture management.

The strengths of this study include the large number of participants, the use of prospectively collected data, and the propensity score matching of variables such as anatomic region, open fracture type, embedded wound contamination, and fracture severity in order to decrease bias. Previous studies on this topic have been retrospective reviews with limited numbers of participants. Additionally, the data utilized in the present study were obtained from multiple hospitals across the world, likely increasing the external validity of our findings.

The main limitation of this study is the subjectivity of the assessment of embedded wound contamination. To limit bias, contamination was graded based on the OTA-OFC¹². However, despite this effort, the severity of wound contamination is not presently quantifiable, and the use of a staged versus fix-and-close treatment was left to the discretion of the treating surgeon. Another limitation of the study is the lack of detail regarding the fracture pattern and

location within the anatomical region as well as the energy level of the injury, which may contribute to the degree of soft-tissue injury and potentially impact fracture healing. Although the treatment groups were propensity score-matched on the basis of fracture pattern severity, accounting for OTA-OFC bone loss, fracture anatomic region, and open fracture type, in order to limit this bias, we were not able to completely negate the inherent bias of different fracture types and patterns within the same anatomic region.

Conclusions

Our findings suggest that adopting fix-and-close in open fractures of type IIIA or lower at the index procedure may not only be safe but also beneficial, even in patients with embedded wound contamination, provided that adequate debridement is performed. Fix-and-close was associated with decreased odds of deep SSI within 90 days and reoperation for infection within 1 year following the index treatment without any increase in wound-healing complications.

Appendix

 Supporting material provided by the authors is posted with the online version of this article as a data supplement at [jbjs.org \(http://links.lww.com/JBJS/1604\)](http://links.lww.com/JBJS/1604). ■

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References

- Hampton OP Jr. Basic principles in management of open fractures. *J Am Med Assoc.* 1955 Oct 1;159(5):417-9.
- Trueta J. "Closed" treatment of war fractures. *Lancet.* 1939;233(6043):1452-5.
- Trueta J. Reflections on the past and present treatment of war wounds and fractures. *Mil Med.* 1976 Apr;141(4):255-8.
- Dubina AG, Morcos G, O'Hara NN, Manzano GW, Vallier HA, Farooq H, Natoli RM, Adams D, Obrebsky WT, Wilkinson BG, Hogue M, Haller JM, Marchand LS, Hautala G, Matuszewski PE, Pechero GR Jr, Gary JL, Doro CJ, Whiting PS, Chen MJ, DeBaun MR, Gardner MJ, Reynolds AW, Altman GT, Obey MR, Miller AN, Haase D, Wise B, Wallace A, Hagen J, O'Donnell J, Gage M, Johnson NR, Karunakar M, Dynako J, Morellato J, Pantan ZA, Gitajn IL, Haase L, Ochenjele G, Roddy E, Morshed S, Sagona AE, Caton TD, Weaver MJ, Westberg JR, Miguel JS, O'Toole RV. Is the timing of fixation associated with fracture-related infection among tibial plateau fracture patients with compartment syndrome? A multicenter retrospective cohort study of 729 patients. *Injury.* 2022 Nov;53(11):3814-9.
- Flagstad I, Albright P, Pedri T, Kleinsmith RM, Schmidt A, Alley M, Westberg JR, Fidel Moreno A, Henry G, Tatman LM, Obrebsky WT, Tornetta P3rd, Cunningham BP. Early versus delayed definitive fixation relative to fasciotomy closure in high-energy tibial plateau fractures with compartment syndrome. *J Orthop Trauma.* 2024 Jun 1;38(6):195-200.
- Benson DR, Riggins RS, Lawrence RM, Hoeprich PD, Huston AC, Harrison JA. Treatment of open fractures: a prospective study. *J Trauma.* 1983 Jan;23(1):25-30.
- DeLong WG Jr, Born CT, Wei SY, Petrik ME, Ponzio R, Schwab CW. Aggressive treatment of 119 open fracture wounds. *J Trauma.* 1999 Jun;46(6):1049-54.
- Jenkinson RJ, Kiss A, Johnson S, Stephen DJG, Kreder HJ. Delayed wound closure increases deep-infection rate associated with lower-grade open fractures: a propensity-matched cohort study. *J Bone Joint Surg Am.* 2014 Mar 5;96(5):380-6.
- Scharfenberger AV, Alabassi K, Smith S, Weber D, Dulai SK, Bergman JW, Beaupre LA. Primary wound closure after open fracture: A prospective cohort study examining nonunion and deep infection. *J Orthop Trauma.* 2017 Mar;31(3):121-6.
- Sprague S, Slobogean G, Wells JL, O'Hara NN, Thabane L, Mullins CD, Harris AD, Wood A, Viskontas D, Apostle KL, O'Toole RV, Joshi M, Johal H, Al-Asiri J, Hymes RA, Gaski GE, Pilson HT, Carroll EA, Babcock S, Halvorson JJ, Romeo NM, Matson CA, Higgins TF, Marchand LS, Bergin PF, Morellato J, Van Demark RE3rd, Potter GD, Gitajn IL, Chang G, Phelps KD, Kempton LB, Karunakar M, Jaeblo T, Demyanovich HK, Domes CM, Kuhn GR, Reilly RM, Gage MJ, Weaver MJ, von Keudell AG, Heng M, McTague MF, Alnasser A, Mehta S, Donegan DJ, Natoli RM, Szatkowski J, Scott AN, Shannon SF, Jeray KJ, Tanner SL, Marmor MT, Matityahu A, Fowler JT, Pierrie SN, Beltran MJ, Thomson CG, Lin CA, Moon CN, Scolaro JA, Amirhekmat A, Leonard J, Pogorzelski D, Bzovsky S, Heels-Ansdell D, Szasz OP, Gallant JL, Della Rocca GJ, Zura RD, Hebden JN, Patterson JT, Lee C, O'Hara LM, Marvel D, Palmer JE, Friedrich J, D'Alleyrand JG, Rivera JC, Mossuto F, Schrank GM, Guyatt G, Devereaux PJ, Bhandari M; PREP-IT Investigators; The PREP-IT Investigators. Skin Antisepsis before surgical fixation of extremity fractures. *N Engl J Med.* 2024 Feb 1;390(5):409-20.
- PREP-IT Investigators. Aqueous skin antisepsis before surgical fixation of open fractures (Aqueous-PREP): a multiple-period, cluster-randomised, crossover trial. *Lancet.* 2022 Oct 15;400(10360):1334-44.
- Orthopaedic Trauma Association: Open Fracture Study Group. A new classification scheme for open fractures. *J Orthop Trauma.* 2010 Aug;24(8):457-64.
- Meinberg EG, Agel J, Roberts CS, Karam MD, Kellam JF. Fracture and Dislocation Classification Compendium-2018. *J Orthop Trauma.* 2018 Jan;32(Suppl 1):S1-170.
- Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med.* 2009 Nov 10;28(25):3083-107.
- Centers for Disease Control and Prevention. CDC/NHSN surveillance definition for specific types of infections. 2025. Accessed 2025 Apr 2. https://www.cdc.gov/nhsn/pdfs/pscmanual/17pscnosinfdef_current.pdf
- Russell GG, Henderson R, Arnett G. Primary or delayed closure for open tibial fractures. *J Bone Joint Surg Br.* 1990 Jan;72(1):125-8.
- Moola FO, Carli A, Berry GK, Reindl R, Jacks D, Harvey EJ. Attempting primary closure for all open fractures: the effectiveness of an institutional protocol. *Can J Surg.* 2014 Jun;57(3):E82-8.