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QUESTION 3: Should open fracture wounds be closed primarily or closed secondarily? If closed primarily, which ones and under what criteria?

RECOMMENDATION: Yes. Primary wound closure of many open fracture wounds appears to be a safe and likely beneficial strategy in the modern setting of improved debridement techniques, better methods of fracture stabilization, and improved utilization of early systemic antibiotic administration. It appears safe for lower grade open fractures and a subset of higher-grade open fractures when the wound is deemed appropriate for primary closure on a clinical basis.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

METHODS

Randomized controlled trials, nonrandomized trials, prospective and retrospective observational studies were eligible for inclusion. We searched Medline, Embase, CINAHL, and the Cochrane Central Register of Controlled Trials (CENTRAL) up to March 2018 for published studies without language restriction. Our search strategy, including keywords and MeSH headings, are provided in the Appendix. Eligible studies met the following criteria: (1) all patients included in the study had an open fracture, (2) infection was an outcome variable and (3) there was a comparison between patients with wounds closed primarily and secondary wound closure. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were followed. The initial search resulted in 303 papers. After removal of duplicates and screening of titles and abstracts, 12 articles were assessed and reviewed.

RATIONALE

The traditional practice of leaving all open fracture wounds open for repeat debridement at a later point in an effort to minimize risk of deep infection has changed over time. Many surgeons now routinely close most open fracture wounds at the time of initial debridement and fixation, particularly in lower grade open fractures and when wound severity and contamination are judged to be appropriate for primary closure.

A systematic review of the literature reveals no level I randomized trials in support of the practice of primary wound closure for open fractures, and the literature supporting this approach is consistently in favor of the practice, but it is also relatively weak. There is a group of more recent studies that has uniformly demonstrated lower surgical site infection rates with primary closure than with secondary closure for various open fractures in adults and children [1–7] and only one older study showing higher infection rates with primary closure [8]. However, all of these studies are methodologically limited as they do not account for selection bias between the less severe wounds that were closed primarily and the more severe wounds that were closed secondarily. As wound severity is very strongly associated with infection rates, this bias is important enough that results from these studies provide only limited insight on this issue except to point out that primary closure of some open fractures does not seem to be associated with high infection rates.

Other authors have provided similar data outlining low rates of infection utilizing a practice of primary wound closure in the vast majority of open fracture cases [9,10]. DeLong et al. used primary closure in 88% of type I, II and IIIA open fractures and had a 4% infection rate [9]. Similarly, Moola et al. used primary closure in 86% of 297 fractures and had a 4.7% deep infection rate [10]. However, while reassuring that primary closure of the majority of open fractures appears to result in an acceptable infection rate compared to historical controls, these studies are similarly methodologically limited as they lack a control group, so it is unknown if a practice of using more secondary wound closures in these patients would have resulted in a higher or lower infection rate.

One double-blind, randomized trial was published in 1993 using a factorial design to compare primary to delayed wound closure as well as the type of antibiotics used [11]. Although the random design is appealing, the sample size of only 82 patients with a low event rate presents a substantial risk of type II error and this study is very underpowered for the outcome of surgical site infection. The cohort only had two deep surgical site infections, so its conclusion that primary closure is safe is reassuring in that there was not a high infection rate in this group, but of limited value in comparing this practice to secondary closure.

The safety of primary closure was also demonstrated in a comparison between two South African trauma centers, one that used primary wound closure and one that did not [12]. This study also concluded that primary closure was safe, but again it was underpowered with a sample size of only 95 patients and an overall infection rate of only 3.3 % (3 patients). Therefore, there is significant risk of type II error with this study, and it therefore cannot provide

sufficient evidence regarding any potential difference in outcomes between the two closure strategies.

Two recent case-controlled studies provide the best evidence in support of this practice while attempting to address the issue of selection bias while also having adequate sample size and event rates to exhibit adequate statistical power. Jenkinson et al. used a propensity-matched cohort study design to demonstrate a lower infection rate in primary wound closure (4%) vs. secondary wound closure (18%, p = 0.0001) even after only including patients matched for likelihood of receiving delayed closure using propensity matching [13]. Scharfenberger et al. collected data prospectively and matched their patients to historical controls from a previous study on factors thought to predict likelihood of surgical site infection and also demonstrated that primary closure had a lower infection risk (4% vs. 9%, p = 0.001) [14]. Although both of these studies are methodologically superior to previous efforts to compare the effect of wound closure strategy on infection rates, the authors point out that there is still risk of unmeasured selection bias and a randomized trial is needed to rigorously compare the efficacy of these two closure strategies.

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APPENDIX – SEARCH STRATEGY (NO PUBLICATION DATE LIMIT)

Ovid Medline – 114 references retrieved on 03/14/2018
((open adj3 fracture*).ab,ti. OR "Fractures, Open".sh.) **AND**
((primary OR delay* OR early OR secondary OR tim* OR definitive OR immediate) adj3 (closure*)).ab,ti **AND**
((infection* or sepsis).ab,ti. or Infection/ or "Wound Infection".sh. or "Cross Infection".sh. or "Sepsis".sh.)

Embase – 147 references retrieved on 03/14/2018
((open NEXT/3 fracture*):ab,ti OR 'open fracture'/de) **AND**
((primary OR delay* OR early OR secondary OR tim* OR definitive OR immediate) NEXT/3 (closure*)):ab,ti **AND**
(infection*:ab,ti OR sepsis:ab,ti OR 'infection'/exp OR 'wound infection'/de OR 'cross infection'/de OR 'hospital infection'/de OR 'sepsis'/exp)

CINAHL – 29 references retrieved on 03/14/2018
((open W3 fracture*) OR MH Fractures, Open) **AND**
((primary OR delay* OR early OR secondary OR tim* OR definitive OR immediate) W3 (closure*)) **AND**
(infection* OR sepsis)

CENTRAL – 13 references retrieved on 03/14/2018 – in Title, Abstract, Keywords
(open NEAR/3 fracture*) **AND**
((primary OR delay* OR early OR secondary OR tim* OR definitive OR immediate) NEAR/3 (closure*)) **AND**
(infection* OR sepsis)

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QUESTION 4: What are the evidence-based recommendations for the use of negative pressure wound therapy (NPWT) in open fractures and traumatic wounds?

RECOMMENDATION: NPWT is an appropriate dressing in the short-term management (< 7 days) of complex traumatic wounds over open fractures, prior to definite soft tissue closure. NPWT is not superior to other sealed dressings and has increased initial cost.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 86%, Disagree: 9%, Abstain: 5% (Super Majority, Strong Consensus)
Note: Please see Question 2 under Section 1.2. Prevention Risk Mitigation for additional rationale regarding NPWT.

METHODS

A comprehensive literature review was performed to identify all studies on the use of NPWT for the treatment of open fractures and traumatic wounds. We searched Ovid Medline, Scopus, and the Cochrane Central Register of Controlled Trials (CENTRAL) up to May 2018 for published studies. The search strategy, including keywords and MeSH headings, are provided in the Appendix. Eligible studies