Concordance Between Traditional Culture and Next Generation Sequencing

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Purpose: Risk of infection in severe open fractures remains unacceptably high and largely unchanged over the last 25 years. This may in part be due to an incomplete understanding of the open fracture microbiome, based presently on culture-based assessment strategies, which have substantial limitations and biases. Because the majority of bacteria remain unculturable, the diversity of complex bacterial communities in inevitably underestimated using standard cultivation methods. Next generation sequencing (NGS) has emerged as a promising technique that is free from many inherent biases and limitations of traditional culture. However, enthusiasm must be tempered by issues around high sensitivity and increased complexity of data requiring interpretation. Based on the increased sensitivity of NGS, we hypothesize that traditional culture results will identify a subset of microbial species identified using NGS. Thus, the aim of the present study is to evaluate the concordance between traditional culture and NGS results.

Methods: This is a secondary analysis of patients enrolled in the METRC Bioburden Study who have sequencing completed (n = 115 total, 63 baseline open fracture patients and 52 follow-up complication patients). Baseline open fracture wound specimens were collected at time of definitive wound closure. NGS and culture were considered concordant when all cultured species are present among NGS-identified species.

Results: Concordance between NGS and culture at the time of open fracture wound closure was only 40%. However, among patients with follow-up specimens during a procedure for a complication (infection or nonunion), NGS and culture concordance was higher at 71%. In patients who had concordant open fracture wound specimens who also went on to develop infection, 72% of infection microbial species were present at time of open fracture wound closure.

Conclusion: The relatively low concordance between NGS and culture in open fractures must be comprehensively explored before NGS can be applied more broadly. These results may be attributed to the difficulty of culturing bacteria from a relatively low bioburden open fracture environment, particularly when compared to the higher concordance in actively infected specimens Furthermore, the high rate of subsequent infection caused by species identified in concordant open fracture wounds corroborates the importance the open fracture microbiome and emphasizes the importance of studying open fracture microbiome using more sensitive and less biased culture-independent assessment strategies.