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Next-Generation Sequencing Results Suggest that a Change in Antibiotic Prophylaxis in Severe Open Tibia Fractures is Warranted

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Purpose: Infection following open tibial fractures has remained relatively unchanged for decades. Antibiotic prophylaxis for open fractures and subsequent surgical procedures is standard of care. However, a 2019 OTA meeting abstract suggests that antibiotics administered at the time of wound closure/coverage in open tibial fractures are ineffective against the bioburden found in most cases based on culture data. Recent non-orthopaedic research suggests that choosing antibiotics based on next-generation sequencing (NGS) data can improve outcomes compared to choices made empirically or based on cultures. We hypothesized that infectious disease (ID) physicians would consider a change in prophylactic antibiotics at time of wound closure/coverage when considering both NGS and culture data compared to culture data alone.

Methods: This is a secondary analysis of the METRC Bioburden study. Of the 646 patients with high-energy tibia fractures that required second debridement surgery and delayed definitive wound closure/coverage, 60 cases had both NGS samples and cultures obtained from the wound at the time of definitive closure/ coverage. A panel of 3 ID experts reviewed the 60 cases to answer the question "would you consider a change in the antibiotic(s) given based on the additional NGS information over culture information alone?". They were provided clinical vignettes, NGS and culture data, and the antibiotics given from 24 h prior to surgery up to 72 h after surgery. The primary outcome was number of cases considered for a change in antibiotics by 2/3 majority or consensus.

Results: The ID physicians determined that in 37% of cases NGS information would have changed prophylactic antibiotic selection at the time of definitive wound closure/coverage. Per physician, the change in antibiotic recommendations was 20, 40, and 73% of cases.

Conclusion: The data suggest that in $\geq 20\%$ of cases the antibiotic prophylaxis given at the time of definitive wound closure/coverage is thought to be inadequate per ID attendings. This information highlights the potential to improve antibiotic prophylaxis protocols in the hopes of decreasing infection rates. Choosing antibiotics is a clinical decision based on a multitude of factors, including ID physician training and preferences, and guided by the patient's clinical scenario. These data indicate obvious variability in ID attending preferences based on bioburden.

The FDA has stated that it is the responsibility of the physician to determine the FDA clearance status of each drug or medical device they wish to use in clinical practice.