

Next-Generation Sequencing as a Valuable Tool for Determination of Causative Microbial Agents in Bone and Soft-Tissue Infections

Aims: Bone and soft-tissue infections (BSTIs) are challenging to diagnose and treat, regularly requiring repeat cultures, serial debridements, and multiple courses of antibiotics. While culture-based detection remains popular, it is challenged by prior antibiotic administration, fastidious organisms, and polymicrobial infections. Moreover, fungal and acid-fast bacilli (AFB) cultures are plagued by extensive turnaround times (TATs). We aim to be the first study to compare organisms, TATs, and costs for next-generation sequencing (NGS) and all four culture modalities in the broad context of orthopedic infections.

Methods: We retrospectively identified and reviewed 26 patients presenting with suspected BSTIs from May 2023-August 2024 to the University of Colorado Hospital Department of Orthopedics. All patients received both NGS and cultures and were analyzed regarding identified organisms, TATs, and cost.

Results: Of the patients, 5/26 (19.2%) received negative NGS results yet positive cultures, 6/26 (23.1%) received positive NGS results yet negative cultures, 7/26 (26.9%) received negative NGS results and cultures, and 8/26 (30.8%) received positive NGS results and cultures. Within the last group, 1/8 (12.5%) had no agreement, 2/8 (25%) had full agreement, and 5/8 (62.5%) had partial agreement. Mean and median TATs in days were as follows: aerobic ($\bar{x} = 4.8$; $\tilde{x} = 5$), anaerobic ($\bar{x} = 9.28$; $\tilde{x} = 7$), fungal ($\bar{x} = 29.9$; $\tilde{x} = 30$), AFB ($\bar{x} = 54.5$; $\tilde{x} = 57$), and NGS collected-to-reported ($\bar{x} = 6.96$; $\tilde{x} = 6$). NGS was 42.5% cheaper than ordering cultures at our institution (\$249 vs. \$433).

Conclusion: NGS is an informative, timely, and economical tool for use alongside culture-based detection in BSTIs. NGS may improve patient outcomes by bypassing fungal and AFB wait times and by providing identification when cultures are negative. Further, NGS highlights rare and difficult-to-culture organisms in polymicrobial infections, the identities of which may be important in the setting of latent and recurring BSTIs.