Diagnostic Characterization of a Newly FDA-Authorized Multiplex Polymerase Chain Reaction Platform for Synovial Fluid Pathogen Detection

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INTRODUCTION:
Efforts to detect pathogens in synovial fluid using molecular amplification techniques have been substantially hampered by the complex trade-off between sensitivity (identifying true positives) and specificity (avoiding false positives). This study aimed to assess the diagnostic characteristics of a newly FDA-authorized multiplex polymerase chain reaction (PCR) platform designed for pathogen identification in synovial fluid.
METHODS:
We conducted a study involving 144 synovial fluid samples submitted to a single clinical laboratory for diagnostic testing including microbiologic culture. The samples met the inclusion criteria for one of three diagnostic cohorts, based on a combination of culture results and the synovial fluid portion of the 2018 International Consensus (ICM) definition of Prosthetic Joint Infection (PJI): 1) Culture-negative and Not Infected (N=55), 2) Culture-positive Infection (N=68), and 3) Culture-negative Infection (N=21). Diagnostic characterization of the PCR platform was completed using standard diagnostic metrics.
RESULTS:
The multiplex PCR platform exhibited a high specificity of 100% (95% Confidence Interval [CI]: 94%-100%), with no false positives recorded (0/55). Its sensitivity in detecting organisms (Culture-positive Infection) targeted by the diagnostic platform was robust, at 94% (95% CI: 81%-99%) (33/35). Moreover, among the 33 samples that were both culture-positive and PCR-positive, there was almost perfect concordance between identified organisms. The only exception was a sample that was culture-positive for *S. aureus*, which was positive for both *S. aureus* and *F. magna* by PCR. Notably, the PCR platform identified an organism in 19% of cases (4/21; 95% CI: 5%-42%) that were classified as culture-negative infections.
When including organisms not targeted by the PCR platform, the sensitivity for detecting an organism in culture-positive infection declined to 50% (95% CI: 38%-62%). This was predominantly attributable to the absence of *S. epidermidis* as a target organism in the multiplex PCR platform.
DISCUSSION AND CONCLUSION:
The multiplex PCR platform demonstrated exceptional sensitivity in detecting the organisms it was intended to detect, and successfully identified pathogens in 19% of culture-negative infection cases. These performance metrics were paired with a strikingly low false-positive rate, a combination of diagnostic features seldom achieved by molecular diagnostic methods in synovial fluid. The addition of *S. epidermidis* as a target organism to the multiplex platform would likely result in a substantial increase in the overall sensitivity for culture-positive and culture-negative PJI.