The Role of Next-Generation Sequencing in the Diagnosis of Shoulder Periprosthetic Joint Infection

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INTRODUCTION: Periprosthetic joint infection (PJI) of the shoulder poses a complex clinical challenge due to the low virulence of the most common causative organisms, namely *C. acnes* and *S. epidermidis*. Many of these infections can be difficult to diagnose even with the use of inflammatory markers, synovial fluid analyses, and fluid and tissue cultures. Next-generation sequencing (NGS) has demonstrated promising diagnostic utility in hip and knee PJI. There is a paucity of data examining this relatively new technology in the context of shoulder PJI. Thus, the purpose of this study was to assess the diagnostic utility of NGS in the setting of PJI following revision shoulder arthroplasty.

METHODS: Patients undergoing revision shoulder arthroplasty were prospectively enrolled. Pre-operative labs, including white blood cell (WBC) count, serum erythrocyte sedimentation rate (ESR), and serum C-reactive protein (CRP) level, were obtained. At the time of surgery, synovial fluid, deep tissue, and swabs were obtained for NGS. Deep-tissue specimens were also sent to the institutional laboratory for culture with extended incubation. The likelihood of infection was determined on the basis of a combination of preoperative clinical findings and serum measurements, intraoperative clinical findings, and intraoperative tissue or fluid culture results. Patients were then classified into one of four possible groups: definite infection, probable infection, probable contaminant, or no evidence of infection. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for NGS by comparing to patients from the definite infection group. Concordance between culture and NGS was defined as complete if NGS correctly identified all organisms on culture.

RESULTS: There were 63 patients with a mean age of 63.6 ± 11.3 years, mean body mass index (BMI) of 31.9 ± 7.5 mg/kg, and 43% were female (n=27) [Table I]. There were 11 patients in the definite infection group, 7 patients in the probable infection group, 2 in the probable contaminant group, 21 in the no evidence of infection group, and 22 that could not be classified into a group due to an elevated ESR and/or CRP without any positive cultures. When comparing the definite infection group with NGS, the sensitivity was 72%, specificity was 83%, PPV was 47%, and NPV was 93%. There were 9 patients with complete concordance, 0 with partial concordance, and 11 patients that were discordant. There were 8 patients that had negative cultures but positive NGS. The organisms identified with NGS were Staphylococcus epidermidis (n=5), Cutibacterium acnes (n=7), Streptococcus mitis (n=1), Staphylococcus aureus (n=1), Escherichia coli (n=1), Serratia marcescens (n=1), and Corynebacterium striatum (n=1).

DISCUSSION AND CONCLUSION:

These results demonstrate that NGS can detect a larger number of bacterial species overall when compared to traditional fluid or tissue culture. Therefore, NGS may be a useful adjunct in identification of causative organism(s) in the diagnosis of shoulder PJI.

Table I. Clinical Characteristics

	Patients (n= 63)
Age (years)	
Mean (SD)	63.6 (11.3)
Range	41 - 87
Sex	
Male (%)	36 (57%)
Female (%)	27 (43%)
Body Mass Index (BMI)	
Mean (SD)	31.9 (7.5)
Range	20.7 – 48
Past Medical History	**n (%)**
Hypertension	44 (69.8)
Diabetes	10 (15.9)
Heart Disease	14 (22.2)
Pulmonary Disease	17 (27.0)
Alcohol Use	27 (42.9)
Tobacco Use	13 (20.6)