Evaluation of the diagnostic utility of universal PCR testing

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BACKGROUND

- Despite massive advances in microbiology laboratory technique, complex infections often represent a diagnostic challenge when attempting to identify the causative organism.
- Traditional cultures may fail to grow microorganisms for a variety of reasons such as inadequate sampling, prior antibiotic use, or the inherent insensitivity of culture methods for fastidious pathogens.
- Molecular testing allows for the detection of microbial nucleic acids directly from clinical specimens and does not require the presence of viable organisms for identification.
- Universal polymerase chain reaction testing (UPCR) is offered though the University of Washington Department of Laboratory Medicine and Pathology as a metagenomic approach using broad-range PCR primers followed by sequencing to hypothetically identify any pathogen present.
- The testing is composed of 3 separate tests for bacterial (BUPCR), fungal (FUPCR), and acid-fast (AFUPCR) organisms.[1]

OBJECTIVES

- To evaluate the diagnostic utility of UPCR by comparing culture and UPCR results, and their impact on management.

METHOD

- A single quaternary care center retrospective chart review of the cohort of patients who had received at least 1 UPCR within a 2-year study period
- Data collected included: type of tissue, UPCR result, traditional culture result, type of antimicrobial therapy before and after UPCR results

RESULTS

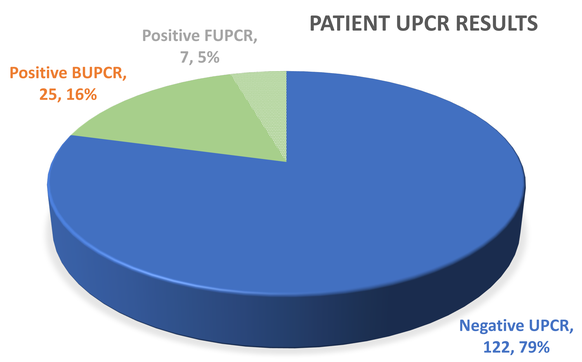

Figure 1: 155 total patients received UPCR testing over the 2 year period. 32/155 (20%) were positive. Of those positive results 25/33 (16%) were BUPCR and 7/33 (5%) were FUPCR. No AFUPCR testing returned positive

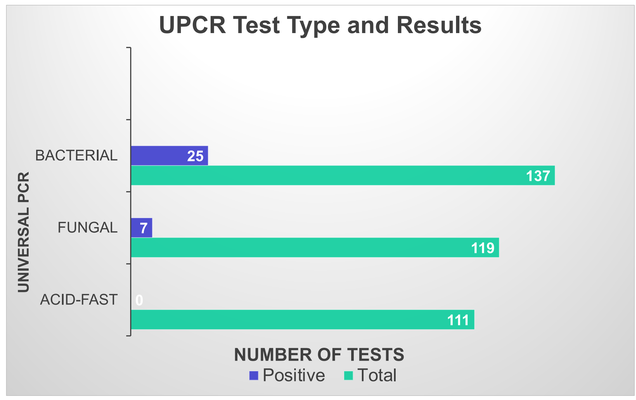

Figure 2: Number of positive UPCR tests compared to the total number of all UPCR tests by test type. On 155 patients we performed 367 UPCR test:. 25/137 BUPCR and 7/119 FUPCR were positive. No AFUPCR tests returned positive.

UPCR n=155	Culture	Patients n=155	Change to Therapy n=8	Impact of UPCR Results on Therapy
Positive n=32	Positive	17	1	1 patient had both tests positive but for different organisms and therapy was changed in favor of BUPCR result. The remainder of the cases had agreement between cultures and UPCR
	Negative	15	4	4 patients had positive BUPCR and negative cultures and therapy was changed according to BUPCR results
Negative n=123	Negative	112	3	Negative UPCR led to antimicrobial discontinuation in 3 patients.
	Positive	11	0	10 negative BUPCR and 1 negative FUPCR did not change therapy in patient with positive cultures

Figure 3: Impact of UPCR test result on therapy plan. Of 155 patients, 32 (20%) had positive UPCR, 8 (5%) had therapy changed based on the UPCR result.

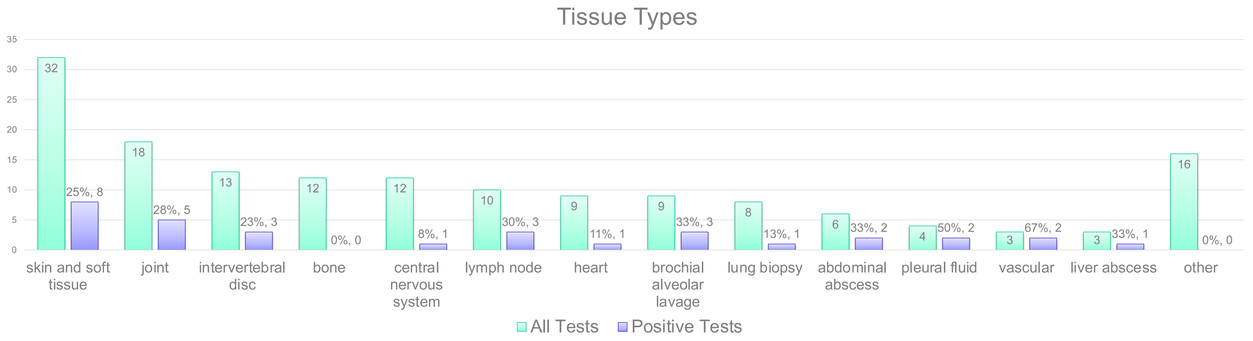

Figure 4: UPCR tests arranged by tissue type and divided into positive and negative results. The largest number of samples were taken from skin and soft tissue (32), joint (18) and intervertebral disc (13), with positivity rate 25%, 28% and 23%, respectively. Interestingly, from 12 samples obtained from bone, none resulted positive.

DISCUSSION

- From 367 tests performed on 155 patients only 32 resulted positive representing 9% test positivity rate and 20% patient positivity rate
- Highest positivity rate was among BUPCR (16%), comparing with FUPCR (5%) and AFUPCR (0%).
- 8/155 tested patients derived benefit from UPCR testing: in 5 antimicrobials were changed based on UPCR results, and in 3 antimicrobials were discontinued after UPCR results confirmed negative culture results. In all 8 of these cases we would expect that the changes significantly impacted patient outcomes through either discontinuation of unnecessary antibiotics or initiation of appropriate therapy.
- Despite the good sensitivity of UPCR testing[2], in 11 patients with positive cultures UPCR test was negative. UPCR results did not change management. Of these 11 tests, only 1 was submitted from a paraffin block, all others were cryopreserved samples.
- Our study has several limitations including a small sample size, retrospective nature and lack of insight into the patient's clinical presentation

CONCLUSION

- Based on the real-world experience, UPCR results have limited impact on antimicrobial management. Further studies are needed to identify clinical scenarios where UPCR may be of greater utility. From our data it appears the benefit UPCR offered our patients was its breadth of identifiable organisms and not necessarily sensitivity.
- This study highlights the importance of quality improvement projects to evaluate new and existing testing modalities to avoid unnecessary testing and decrease cost burden.

References

1. "Available Tests." *Available Tests | University of Washington Laboratory Medicine: Molecular Diagnosis, Microbiology Division*, University of Washington, https://depts.washington.edu/molmicdx/mdx/available_tests.shtml.
2. Salipante SJ, Sengupta DJ, Rosenthal C, Costa G, Spangler J, et al. (2013) Rapid 16S rRNA Next-Generation Sequencing of Polymicrobial Clinical Samples for Diagnosis of Complex Bacterial Infections. PLOS ONE 8(5): e65226. https://doi.org/10.1371/journal.pone.0065226