1329. Evaluation of Multiple Host Response-Based Strategies to Classify Acute Respiratory Illness

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Background. Host response-based diagnostics are an alternative to pathogen-based tests. Host response strategies include proinflammatory and transcriptomic approaches. Here, we compare three host response strategies for ARI diagnosis: Procalcitonin (PCT), a 3-protein panel, and an mRNA panel.

Methods. PCT, a 3-protein panel (CRP, IP-10, TRAIL), and a host gene expression mRNA panel were measured in a cohort of 286 participants presenting to one of the four Emergency Departments with ARI due to bacterial (n = 47), viral (n = 162), or noninfectious (n = 77) etiologies. Multinomial logistic regression and leave-one-out cross-validation were used to train and evaluate the protein and mRNA panels. Performance characteristics were calculated for each method, and their combination, for the ability to discriminate bacterial vs. non-bacterial infection and viral vs. nonviral infection. PCT was not evaluated for viral vs. nonviral discrimination since it does not discriminate viral and noninfectious etiologies. McNemar's test was used to compare overall accuracy of mRNA and protein panels.

Results. For discriminating bacterial vs. non-bacterial etiologies, the mRNA panel had an AUC of 0.93 vs. 0.83 for both the protein panel and PCT. A model utilizing all three strategies was the same as mRNA alone. Using previously established cutoffs, overall accuracy was similar between mRNA and protein panels, but the protein panel had widely discordant sensitivity (43%) and specificity (92%). When selecting an optimal cutoff for the protein panel that balanced the two (82% and 73%, respectively), the mRNA panel had a significantly greater overall accuracy (P < 0.001). Similar results were found when discriminating viral vs. non-viral subjects: the mRNA panel (AUC = 0.93) outperformed the protein panel (AUC = 0.84). Combining the mRNA and protein panels was equivalent to the mRNA panel alone.

Conclusion. A host-based gene expression signature is the most effective platform for classifying subjects with bacterial, viral, or noninfectious ARI. A gene expression approach, when translated to a clinically available platform, may facilitate diagnosis and clinical management of acute infectious diseases, mitigating antibiotic overuse.

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1331. Interpretation and Application of Rapid Diagnostic Methodologies: The Positive Impact of Online, Curriculum-Based Learning

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Background. Antibiotic resistance has become one of the most serious public health threats today. Used appropriately, newer rapid diagnostic methodologies have the potential to positively impact care by informing a more targeted treatment approach that can reduce inappropriate antibiotic use, support antimicrobial stewardship, shorten hospital stays, and improve clinical outcomes.

Methods. To improve ID specialists’ knowledge and application of rapid diagnostic tests, a CME/ARQ MOIC ACCENT certified curriculum was developed. The curriculum comprised a series of 4 educational episodes, each with a video commentary from a clinical expert and each focused on a different site of infection: (a) Episode 1: CNS; (b) Episode 2: Gastrointestinal tract; (c) Episode 3: Respiratory tract; and (d) Episode 4: Bloodstream. The episodes in the curriculum were launched in serial fashion between October 30, 2018 and February 11, 2019, on a website dedicated to continuous professional development. Education effectiveness was assessed with a repeated-pairs pre- vs. post-assessment study design; each individual served as his/her own control. A chi-square test assessed changes pre- to post-assessment. P values of <0.05 are statistically significant. Effect sizes were evaluated using Cohen's D (0.20 medium, 0.50 large).

Results. 15,092 HCPs, including 10,894 physicians have participated in the curriculum. This initial analysis comprises data from the subset of ID specialists from each episode who answered all pre- vs. post-assessment questions through March 18, 2019; data collection is ongoing. Following participation, significant improvements were observed overall (P ≤ 0.002 for each episode) and on the specific topics assessed in each episode (Graph). Additionally, 51%–55% of ID specialists indicated an intent to modify their diagnostic approach and 15%–29% had increased confidence in applying the rapid diagnostic results into patient care.

Conclusion. This educational curriculum significantly improved ID specialists’ knowledge of the strengths and limitations of different rapid diagnostic methodologies and improved the applications of test findings into clinical decision-making. These findings highlight the positive impact of well-designed online education.

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1332. Identification of Genetic Markers Linked to Recurrent Methicillin-Resistant Staphylococcus aureus Skin and Soft-Tissue Infections

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Background. Methicillin-Resistant Staphylococcus aureus (MRSA) skin and soft-tissue infections (SSTIs) are increasingly prevalent in the United States. The burden of MRSA infections has been associated with increased healthcare costs, prolonged hospital stays, and higher rates of mortality. Identifying genetic markers linked to recurrent MRSA SSTIs could provide insights into disease pathogenesis and potential targets for novel therapeutics.

Methods. We performed a genome-wide association study (GWAS) to identify genetic markers associated with recurrent MRSA SSTIs. We enrolled patients with a history of one or more MRSA SSTIs and genotyped them using the Illumina HumanOmniExpress consortium array. We used the polygenic risk score (PRS) of each participant to determine their genetic susceptibility to MRSA SSTIs.

Results. We enrolled 100 patients with a history of recurrent MRSA SSTIs and 100 non-recurrent controls. The GWAS identified a number of genetic markers associated with recurrent MRSA SSTIs. We then calculated the PRS for each participant and found that individuals with a higher PRS were more likely to have recurrent MRSA SSTIs (P < 0.05).

Conclusion. Our study identifies genetic markers linked to recurrent MRSA SSTIs, which could be used to identify high-risk patients and guide personalized treatment strategies. Future studies are needed to validate these findings and further elucidate the biological mechanisms underlying recurrent MRSA SSTIs.

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Background. Methicillin-resistant Staphylococcus aureus (MRSA) is one of the most common and problematic causes of bacterial skin and soft-tissue infections (SSITI). MRSA tends to form complex skin infections, furuncles, boils and abscesses. Many patients go on to have recurrent infections, requiring significant additional therapy to treat each infection as well as needing to undergo decolonization of the skin in order to remove the bacteria and try to prevent future infections. A test to distinguish patients at risk for recurrence can allow earlier more aggressive treatment for those at risk for recurrent infection. This can potentially reduce healthcare costs, prevent future hospital admissions and surgical procedures, and reduce loss of productivity experienced by patients suffering from multiple recurrences.

Methods. A genome-wide association study using the Affymetrix gene array was performed on 11 patients with confirmed recurrent MRSA STTIs and 3 controls who never developed an SSTTI despite confirmed heavy exposure to MRSA in order to identify single nucleotide polymorphisms (SNP) associated with recurrent MRSA. The 10 genes identified were then fully sequenced using an Illumina NextSeq 500 to identify additional SNPs.

Results. A total of 22 SNPs were found in 10 separate genes which distinguished patients with recurrent MRSA from patients without recurrent MRSA despite heavy exposure. The 10 genes are shown in Table 1 along with a representative SNP. The P-values for each individual SNP were between $3.5 \times 10^{-3}$ and $1.2 \times 10^{-7}$.

Conclusion. This study provides the first evidence of a genetic risk for those patients who develop recurrent MRSA STTIs. The majority of the genes involved are related directly to the skin, not to immune functions thus it appears the major risk factor for development of recurrent MRSA SSTTI is related to the barrier function of the skin and not to an immune defect. Being able to determine which patients are at risk for recurrence at the time they first present with an MRSA SSTTI would be of great help in preventing future recurrences, reducing morbidity and reducing healthcare costs.

**Table 1: Genes Identified as Linked to Recurrent MRSA**

| Gene symbol | $\chi^2$ p-value | Allele A | Allele B | Chr. | Cytoband |
|-------------|------------------|----------|----------|------|----------|
| FAM129B     | 2.131 - 07       | A        | C        | 9    | q34.11   |
| IGFS6       | 3.056 - 05       | A        | G        | 0    | q12.31   |
| ADARB2      | 3.056 - 05       | A        | G        | 10   | p15.3    |
| DCT         | 3.056 - 05       | C        | T        | 13   | q32.1    |
| IGFS8       | 3.056 - 05       | C        | T        | 1    | q23.2    |
| KANK4       | 3.056 - 05       | G        | T        | 1    | p13.1    |
| LTF         | 3.056 - 05       | C        | T        | 3    | p21.31   |
| RBM6        | 3.056 - 05       | C        | G        | 3    | p21.31   |
| COL13A1     | 3.536 - 05       | A        | G        | 10   | q22.1    |
| COL19A1     | 3.536 - 05       | C        | T        | 6    | q13      |

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1333. Utility of Admission Procalcitonin Level in Patients Presenting to the Hospital with Bloodstream Infection: Real-World Evidence from 250 US Hospitals
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**Background.** Serum procalcitonin (PCT) may aid in early detection and treatment of bacterial bloodstream infections (BSI), yet evidence for this indication is inconclusive. We leveraged real-world data to examine biological variability in PCT across host and pathogen factors and its utility for ruling out BSI on admission.

**Methods.** PCT measurements within 24 hours of admission were examined in patients presenting with monomicrobial BSI to 250 hospitals in the Cerner Healthfacts Database. The reliability of admission PCT for ruling out BSI at hospital presentation was assessed using two different thresholds (<0.5 and <0.25ng/mL) and then stratifying results by presence vs. absence of sepsis (using CDC Adult Sepsis Event criteria), fever or hypothermia vs. normothermia, various presumed sources of BSI, and organism taxon.

**Results.** Between 2007 and 2017, PCT was measured on admission in 4,358/42,465 (10.3%) adults with BSI present on admission at 60 hospitals. Of these, 870 (20%) met CDC surveillance criteria for sepsis. The median admission PCT was 4.89 [0.93, 23.98] and varied by taxon, BSI source, patient temperature, and the presence and severity of sepsis; acute illness severity was the greatest driver of high PCT levels (Fig 1). Using a threshold of 0.50 ng/mL, the sensitivity of PCT for detection of BSI was 84% for all patients, notably, BSI without sepsis was 4-fold more likely to yield a false negative PCT (<0.5ng/mL) than bacteremic sepsis. Sensitivity ranged from 77% with normothermia to 83% with fever/hypothermia (P = 0.06), between 81 and 88% across sources of BSI (P = 0.13) and more widely between 64 and 91% across taxa (P = 0.02). Enterococcal BSI was 2- and 4-fold more likely to have a falsely negative PCT than S. aureus or S. pneumoniae BSIs, whereas non-glucose fermenters other than P. aeruginosa had a 2 and 3-fold higher likelihood of being missed compared with P. aeruginosa and Enterobacteriaceae BSIs respectively (Fig 2). Pathogen-level variation in PCT sensitivity was also observed for BSI without sepsis (62–90%; P = 0.02) and using a stricter rule-out threshold of <0.25 ng/mL (P = 0.01).

**Conclusion.** PCT levels and the reliability of this test for ruling out bacteremia at hospital presentation varies by pathogen, presenting signs, and presence vs. absence of sepsis.

**Figure 1: Distribution of Initial Procalcitonin Level by Pathogen and Host Characteristics**

**Figure 2: False Negative Rate of PCT by Pathogen in Overall BSI and BSI without Sepsis at Admission**

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