6-2020

Resolution of a modified CDC definition for carbapenem resistant enterobacteriaceae (CRE) using a rapid multiplex, cartridge-based molecular assay for the confirmation of carbapenemase genes

Harshita Mehrotra
Henry Ford Health, hmehrot1@hfhs.org

Laura Favazza

Brie Kezlarian

Randal Fowler

Nancy Hanson

See next page for additional authors

Recommended Citation

Mehrotra H, Favazza L, Kezlarian B, Fowler R, Hanson N, and Tibbetts R. Resolution of a modified CDC definition for carbapenem resistant enterobacteriaceae (CRE) using a rapid multiplex, cartridge-based molecular assay for the confirmation of carbapenemase genes. Modern Pathology 2020; 33(3):1880-1881.

Authors
Harshita Mehrotra, Laura Favazza, Brie Kezlarian, Randal Fowler, Nancy Hanson, and Robert J. Tibbetts

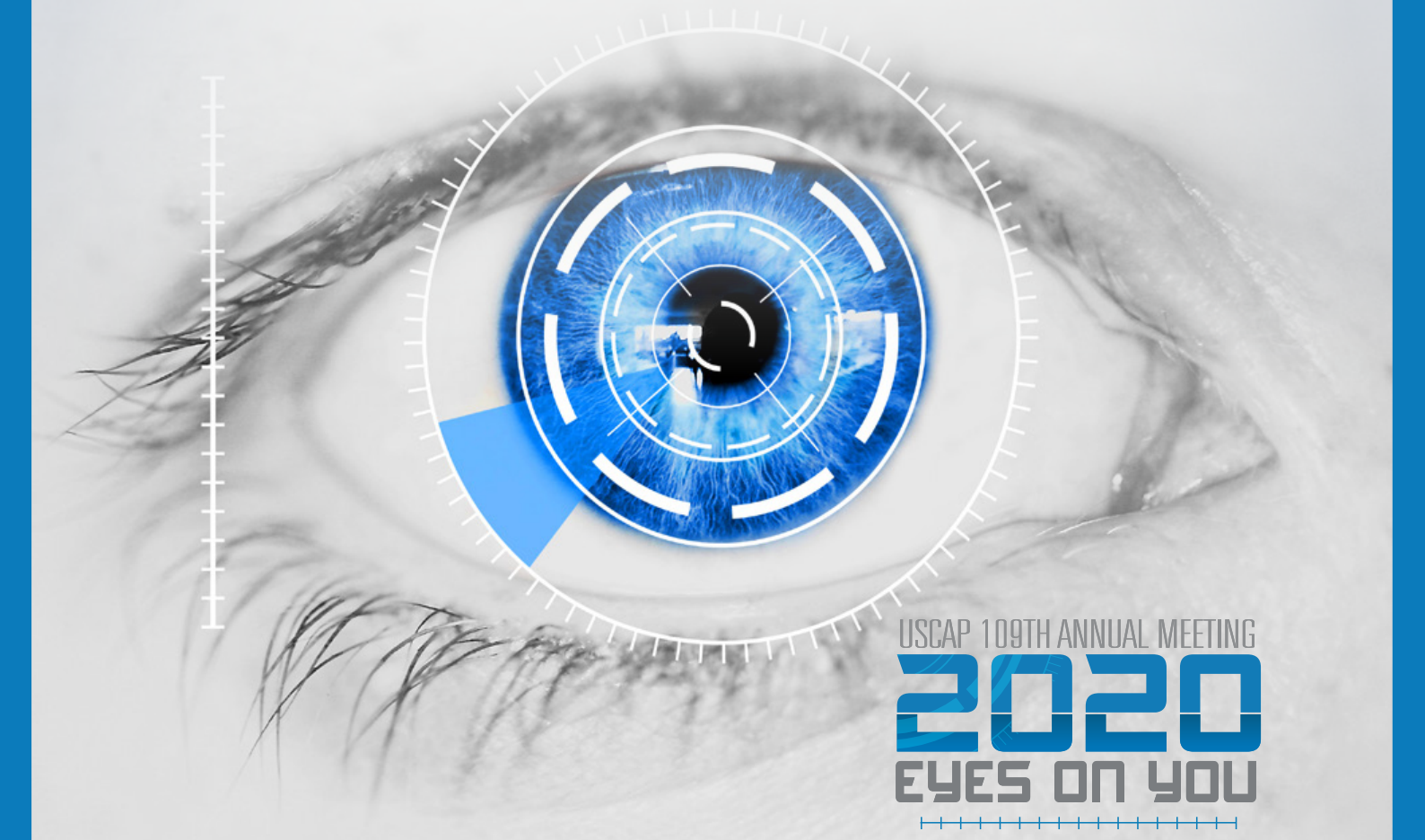
VOLUME 33 | SUPPLEMENT 2 | MARCH 2020

MODERN PATHOLOGY

ABSTRACTS

QUALITY AND PATIENT SAFETY

(1981-2063)



FEBRUARY 29-MARCH 5, 2020

LOS ANGELES CONVENTION CENTER
LOS ANGELES, CALIFORNIA

Published by
SPRINGER NATURE
www.ModernPathology.org

USCAP Creating a Better Pathologist
AN OFFICIAL JOURNAL OF THE UNITED STATES AND CANADIAN ACADEMY OF PATHOLOGY

2031 Resolution of a Modified CDC Definition for Carbapenem Resistant Enterobacteriaceae (CRE) Using a Rapid Multiplex, Cartridge-Based Molecular Assay for the Confirmation of Carbapenemase Genes

Harshita Mehrotra[1], Laura Favazza[2], Brie Kezlarian[3], Randal Fowler[4], Nancy Hanson[4], Robert Tibbetts[5]
[1]Henry Ford Health System, Detroit, MI, [2]University of Pittsburgh Medical Center, Pittsburgh, PA, [3]Memorial Sloan Kettering Cancer Center, New York, NY, [4]Creighton University, Omaha, NE, [5]Henry Ford Heath System, Detroit, MI

Disclosures: Harshita Mehrotra: None; Laura Favazza: None; Brie Kezlarian: None; Randal Fowler: None; Nancy Hanson: *Advisory Board Member*, Streck; Robert Tibbetts: None

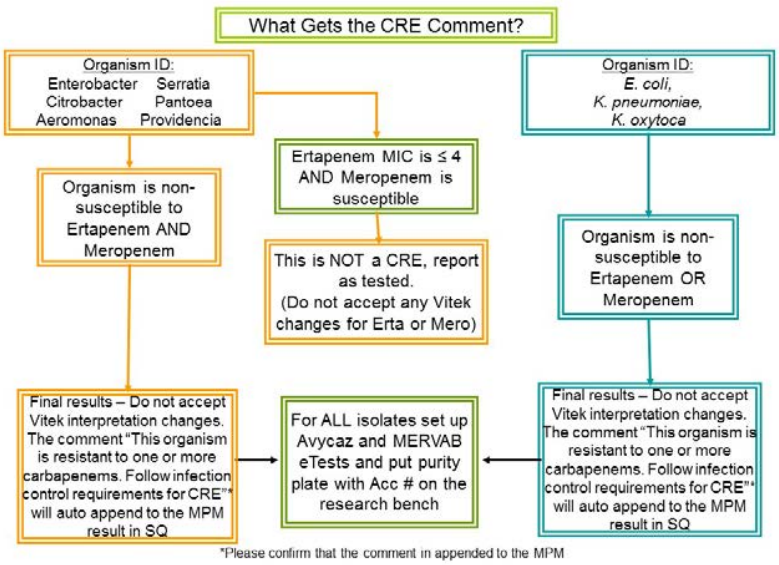
Background: CRE have emerged as a global threat due to their potential to cause invasive infections, often with high mortality rates and are primarily healthcare, associated, with a potential for spread to community settings. The CDC updated its definition of CRE as resistant to a carbapenem: MIC of ≥4 ug/ml for doripenem, meropenem, or imipenem, ≥2 ug/ml for ertapenem, OR documented to produce a carbapenemase. CRE are resistant to carbapenems primarily through the expression of carbapenemase genes (CP-CRE) carried on plasmids, which are easily transferrable hence the CDC recommendation to isolate patients with CP-CRE. However, production of AmpC/ESBL β-lactamases with a decrease of outer membrane proteins (OMP) (non-CP-CRE) can also lead to a higher ertapenem MIC, of which OMPs are not transferable but meet the CDC definition for CRE. The purpose of this study was to develop an algorithm to differentiate CP-CRE from non-CP-CRE using carbapenem MIC and confirmation by a rapid molecular assay.

Design: Genetic and phenotypic testing was performed on 61 isolates of Enterobacteriaceae with MICs to ertapenem ranging from <0.25 ug/ml to >64 ug/ml using PCR to detect *bla*$_{KPC}$, *bla*$_{AmpC}$ and *bla*$_{ESBL}$, and SDS-PAGE to determine OMP production. These data were used to create an algorithm to define CRE in our lab using MIC, the presence of resistance genes and/or OMP production. 40 isolates, including positive and negative controls, with known antibiotic susceptibilities were defined by this algorithm and confirmed by commercially available FDA approved rapid multiplex PCR for carbapenemase genes.

Results: Using this algorithm, we observed 5 discordant PCR results giving us 85% concordance. However, we believe that 3 of these were due to loss of plasmids by repeated freeze-thaw cycles and intend to reanalyze MICs to confirm this. On eliminating these 3 isolates, we have 93% concordance.

	Commercial Mulitplex Molecular Assay	
CRE defined by algorithm	**Carbapenemase detected**	**Carbapenemase not detected**
CP-CREs	20	3
non-CP-CREs	2	15

Figure 1 - 2031



Conclusions: A combination of the CDC definition for CRE and lowered breakpoints to ertapenem led to overcalling non-CP-CRE as CP-CRE may have resulted in inappropriate patient isolation, which is known to have negative patient outcomes and increase costs. Implementation of a multiplex PCR to rule out carbapenemases in isolates with elevated ertapenem but susceptible meropenem MICs resulted in a more sensitive and specific identification of CP-CRE.

2032 STAS Tumor Status is a Reproducible Prognosticator Among Practicing Pathologists

Veronica Merelo Alcocer[1], Negar Rassaei[2], Christopher Febres-Aldana[3], Monica Recine[3], Robert Poppiti[4], John Varlotto[5]
[1]Penn State Health Milton S. Hershey Medical Center, Hershey, PA, [2]Penn State, Hershey, PA, [3]Mount Sinai Medical Center, Miami Beach, FL, [4]Mount Sinai Hospital, Miami Beach, FL, [5]UMass Memorial Medical Group, Worcester, MA

Disclosures: Veronica Merelo Alcocer: None; Negar Rassaei: None; Christopher Febres-Aldana: None; Monica Recine: None; Robert Poppiti: None; John Varlotto: None

Background: "Spread through airspace" (STAS) is defined as the spread of tumor cells into airspaces in the lung parenchyma adjacent to and beyond the edge of the main tumor. It is a newly recognized pattern of invasion reported in adenocarcinoma and squamous cell lung carcinoma . Higher STAS has been reported to be more commonly seen in patients with solid and micropapillary predominant invasive adenocarcinoma, pleural and lymphovascular invasion, and tumor size of 10 mm or larger. Also, STAS has been considered to be an important risk factor for locoregional and distant recurrence in small adenocarcinomas treated by limited resection. In this study, we aim to evaluate if the observer (pathologists) is a determinant of the STAS tumor status.

Design: All primary lung cancer reports from January 1, 2018 to August 1, 2019 were reviewed. A total of 247 CAP Tumor Summaries were completed by our group of 8 general surgical pathologists, two of whom with interest in pulmonary pathology (pathologists 2 and 4). In addition to reporting variability among pathologists, we evaluated the relation between STAS and histologic type, tumor size and grade, and type of resection (lobectomy and wedge resection). This analysis was performed using a multivariate regression analysis conducted in SPSS® (version 22.0; Chicago, Illinois, USA).

Results: STAS, was reported in 128 CAP summaries (52%). Only 2 of the pathologists reported STAS in all cases (pathologists 2 and 4). The rate of positivity for rare reporters, pathologists 3, 6 and 8 was higher (66.66%) than the frequent reporters, pathologists 2 and 4 (26%), suggesting that rare reporters evaluated STAS when it was present in selected cases. Overall, when comparing frequent reporters (pathologists 2 and 4) with all the other pathologists (1, 3, 5, 6, 7, 8), the positivity rate is not significantly different (27.27% vs. 24.13%, respectively). Growth pattern was the only variable showing a significant association with the presence or absence of STAS in multivariate analysis (Figure 1 and Table 1).

Figure 1 - 2032

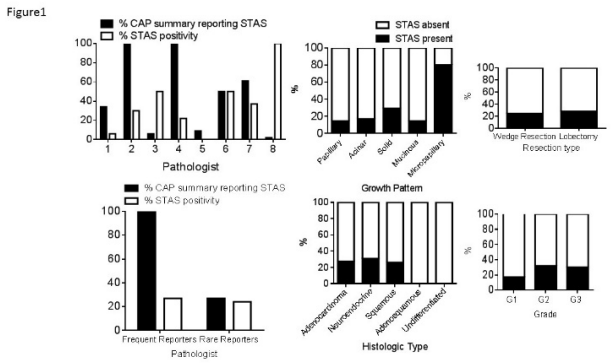


Figure 2 - 2032

Table 1. Multivariate linear regression analysis for STAS as the dependent variable

Variable	Standarized coefficient (β)	P-value	Partial Correlation
Pathologist	0.033	0.708	0.034
Growth Pattern	**0.307**	**0.001**	**0.300**
Histologic type	-1.539	0.126	-0.138
Tumor Grade	0.136	0.131	0.136
Resection type	0.045	0.535	0.048

Conclusions: This fit regression multivariate model demonstrates that the presence or absence of STAS is more likely to be determined by the variable growth pattern with no significant contribution of other variables. As expected for a parameter with high reproducibility, this result affirms that the observer (pathologist) is not significantly influencing the likelihood of STAS to be positive or negative.