



New Guidelines, Less Guidance, and the End of an Era: Healthcare-Associated Pneumonia in 2016

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Keywords

Healthcare associated pneumonia, Pneumonia, Bacterial resistance, Antimicrobial stewardship

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Pneumonia is a leading cause of hospitalization and mortality in the United States [1]. Since the publication of the Infectious Diseases Society of America (IDSA) pneumonia guidelines in 2005, healthcare practitioners have classified patients with pneumonia as having community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP) or healthcare-associated pneumonia (HCAP). The recent HAP/VAP IDSA guideline updated in 2016 put forth a number of changes from the previous version. Amongst the changes is the removal of the concept of HCAP, as it is no longer considered in the spectrum of HAP and VAP [2]. This marked change reflects a paradigm shift in how we manage pneumonia in a day of increasing bacterial resistance and attention to antimicrobial stewardship.

The 2005 guidelines recommended classification of patients based on their risk of infection by resistant bacterial pathogens. The now abandoned HCAP entity included any patient hospitalized in an acute care hospital for two or more days within 90 days of the infection; residing in a nursing home or long-term care facility; exposed to recent intravenous antibiotic-therapy, chemotherapy, or wound care within the past 30 days of the current infection; or on hemodialysis. The extensive definition, based primarily on healthcare exposure, categorized a large population as being at risk for multidrug resistant organisms (MDRO) and drove prescribing practices for pneumonia. These previous guidelines were aimed at appropriately ensuring patients at risk for MDRO are adequately treated early on in the course of their illness [1], however, they lack specificity and often lead to unneeded use of broad spectrum agents. Since its inception in 2005, studies have identified the poor specificity of HCAP as a predictor of MDRO identification in patients with pneumonia [3,4]. The updated 2016 HAP/VAP guidelines have removed the concept of HCAP and recommend use of institution-specific antibiograms to guide empiric antibiotic selection. These updates were made in an effort to curb antibiotic resistance and reduce overuse of vital antibiotics [2].

The concept of HCAP has become increasingly controversial as data concerning its correlation with MDRO and increased mortality

have varied across the literature [5-7]. HCAP categorization includes a broad group of patients who have come into contact with the healthcare system. Previously, it was thought that this healthcare contact was the primary driver of infection due to MDRO pathogens typically associated with causing hospital-acquired infections [1]. Following publication of the 2005 guidelines, a substantial increase in the use of broad-spectrum antibiotics to address the presumed risk of MDROs in HCAP patients was observed. Jones and colleagues evaluated consumption of key antimicrobials following inception of the HCAP concept, finding use of vancomycin and piperacillin-tazobactam nearly doubled from 16% to 31% and 16% to 27%, respectively, from 2006 to 2010 in a United States pneumonia cohort. During the same time period, they observed a decrease in the use of ceftriaxone and azithromycin. These trends exemplify the shift towards use of broad-spectrum therapy as recommended for HAP/VAP regimens and a decrease in the use of traditional CAP regimens. The study also suggests that the increase in broad-spectrum antibiotics was not correlated with an increase in the incidence of resistant organisms but rather, a decreased threshold for initiating broad empiric antimicrobial therapy. In fact, the proportion of patients with cultures positive for MRSA decreased from 2.5 to 2.0% and the number of patients with *Pseudomonas aeruginosa* remained stable (1.9% to 2.0%) during the study period [8].

Considering the many issues of pneumonia classification, Gross and colleagues conducted a retrospective, observational, cohort study to address the epidemiology of CAP and HCAP. The study found that MDROs were uncommon in both the CAP (1.9%) and HCAP (5.9%) populations, and that HCAP did not predict MDRO isolation (odd ratio = 1.95; 95% confidence interval, 0.66 to 5.80; P = 0.23). This study further suggests underlying patient characteristics and local epidemiology may be better predictors of MDRO acquisition, and empiric anti-MRSA and anti-pseudomonal treatment may not be necessary for all HCAP patients [4]. These findings are similar to an earlier cohort study suggesting the incidence of resistant organisms are low in both HCAP and CAP groups [9]. Furthermore, a 2014 systematic review and meta-analysis from Chalmers and colleagues concluded that the concept of HCAP is based on low-quality evidence and does not accurately identify patients at risk for resistant pathogens. The number needed to treat for one patient to benefit from an HCAP regimen compared to a CAP regimen varied widely across the studies: 4-499 for MRSA, 5-330 for *Pseudomonas aeruginosa*, and 6-282 for *Enterobacteriaceae*. These variations further reveal that HCAP is a poor discriminator for MDR pathogens and many patients can be

Citation: Jacob J, Crotty M (2016) New Guidelines, Less Guidance, and the End of an Era: Healthcare -Associated Pneumonia in 2016. Int J Respir Pulm Med 3:063e

Received: October 29, 2016: **Accepted:** November 24, 2016: **Published:** November 28, 2016

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Table 1: Select risk factors for MRSA and Pseudomonas in community-onset pneumonia.

| Organism | Risk Factor | Evidence Summary |
|-------------|------------------------------|--|
| MRSA | Hemodialysis | Observational cohort (prospective): Identification of dialysis during the preceding 30 days as a risk factor for MRSA among CAP/HCAP patients [11] |
| | Prior influenza | Observational cohort and case-series (retrospective): Influenza association with subsequent MRSA pneumonia [12-14] |
| | Illicit drug use | Observational cohort and a case-control study (retrospective): identification of illicit drug use as a risk factor associated with MRSA [15,16] |
| | COPD | Observational cohort and case-control study (retrospective): COPD identified as a risk factor for MRSA pneumonia [15,17] |
| | Prior antibiotic therapy | Observational cohorts and a case-control study (prospective and retrospective): antibiotic exposure within 90 days of pneumonia occurrence associated with MRSA pneumonia [11,15,17] |
| | Prior hospitalization | Observational cohort (prospective): identification of hospitalization for two days or more during the preceding 90 days as a risk factor for MRSA among CAP/HCAP patients [11,15] |
| Pseudomonas | COPD/structural lung disease | Observational cohorts (prospective and retrospective): COPD and structural lung disease associated with <i>Pseudomonas</i> pneumonia [17,18] |
| | Prior antibiotic therapy | Observational cohort (retrospective): antibiotic exposure within 90 days of pneumonia occurrence associated with <i>Pseudomonas</i> pneumonia [17] |
| | Prior hospitalization | Observational cohort (prospective): identification of hospitalization for two days or more during the preceding 90 days as a risk factor for <i>Pseudomonas</i> pneumonia [17,18] |

*MRSA infection not limited to pneumonia.

appropriately treated with narrower spectrum agents. Moreover, the meta-analysis found mortality in HCAP is not increased when age and comorbidities are adjusted for (OR, 1.20; 95% CI: 0.85-1.70; P = 0.30) [10]. All of these findings suggest that the broad definition of HCAP lacks specificity and individual patient-specific factors must be considered when selecting an optimal empiric antibiotic treatment regimen for hospitalized patients with pneumonia.

With the removal of the HCAP concept, greater than 20% of hospitalized patients with pneumonia are not specifically addressed by current guideline recommendations [5]. This population, previously categorized as having HCAP, presents a challenge to clinicians as no clear guidance exists for how best to treat patients with community-onset pneumonia. An update to the CAP guidelines is ongoing and may explicitly address the current gap but, uncertainty abounds in the interim. A number of studies have suggested factors more strongly associated with a MDRO infection include: antibiotic use within 90 days, hospitalization within 90 days, severe pneumonia or critical illness, history of a prior MDRO infection within the past year, or poor functional status [10,11]. However, defining poor functional status is imprecise and varies across the literature. This concept has largely been studied in nursing home patients but, heterogeneity in facility type (e.g., skilled nursing facility, long term care facility) has hindered exact identifying attributes. Among community-onset pneumonia patients with the more strongly MDRO associated risk factors, it may still be necessary to empirically treat with broad-spectrum antibiotic therapy. **Table 1** highlights select risk factors that may necessitate including an anti-MRSA or anti-pseudomonal agent. These risk factors may allow practitioners to more specifically tailor empiric regimens based on specific patient characteristics. In some instances, patients may best be treated with a hybrid regimen (including either anti-MRSA or anti-pseudomonal agent but not both). Use of local epidemiology may also benefit clinicians in directing empiric pneumonia therapy, but the impact of this methodology is largely unknown. Nevertheless, it is clear that further study of risk stratification and optimal empiric antibiotic use in pneumonia is needed.

The era of pneumonia treatment, largely driven by the concept of HCAP is slowly coming to an end. With the publication of the 2016 HAP/VAP IDSA guidelines, we are left with little guidance on how to treat these patients previously diagnosed with HCAP. De-escalation of antibacterial therapy based on pathogen identification is crucial in deterring the collateral damage of broad spectrum antibiotic use both now and in the future, but it is a far cry from the needed steps to preserve the antibiotics we have while optimally treating patients. Undoubtedly advances in timely diagnostic technologies to improve pathogen identification for individual patients are desperately needed. While we await diagnostic advances and further guidance in treating community-onset pneumonia, critical evaluation of individual patient characteristics is warranted. Consideration of patient risk

factors for MDRO and severity of illness, along with institutional and community epidemiology, may allow for more personalized and ultimately improved pneumonia management.

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