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REVIEW

Managing CAP patients at risk of clinical failure

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Summary
Community-acquired pneumonia (CAP) is a curable disease. Both the European and American clinical practice guidelines provide algorithms how to manage patients with CAP.

However, as populations worldwide are ageing and bacteria are becoming multidrug resistant, it is necessary to address the major factors that put patients at risk of poor outcome. These may include age, comorbidities, the settings where pneumonia was acquired or treated, the need for hospitalisation or ICU admission, likely causative pathogen (bacteria or virus) in a certain region and their local susceptibility pattern. One complicating fact is the lack of definite causative pathogen in approximately 50% of patients making it difficult to choose the most appropriate antibiotic treatment. When risk factors are present simultaneously in patients, fewer treatment options could be rather challenging for physicians. For example, the presence of comorbidities (renal, cardiac, hepatic) may exclude certain antibiotics due to potential adverse events.

Assessing the severity of the disease and monitoring biomarkers, however, could help physicians to estimate patient prognosis once diagnosis is confirmed and treatment has been initiated. This review article addresses the most important risk factors of poor outcome in CAP patients.

Contents

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Introduction

Community-acquired pneumonia (CAP) is one of the most common infectious diseases and a major cause of morbidity and mortality worldwide [1], and is the most common infectious cause of death in the developed world [2,3] with rates as high as 48% [2,4,5]. Although CAP can occur at any age, in the past few decades, the epidemiology of CAP has undergone a marked shift and patients are now presenting at an increasingly older age [6]. For this reason, the occurrence of CAP in developed countries is likely to increase in the coming years due to the ageing populations [2,7].

While 50—80% of adult CAP patients are treated on an ambulatory basis, hospitalisations are common, particularly among the elderly [8—10] with admissions being highest among patients over the age of 65 years [2,10,11]. The high rate of hospital admission, prolonged stay in hospital and long periods of inactivity associated with CAP lead to considerable socioeconomic burden [2,3]. In addition, comorbidities are common in CAP patients and increase the risk of mortality and hospitalisation [12].

However, hospitalisation rates have fallen in recent years following recent developments in the use of biomarkers and prognostic tools to predict disease severity [12—16], advances in antibiotic therapy [17—19] and inclusion of criteria for hospitalisation in current guidelines for the management of CAP patients [20].

Identification of patients at risk of poor outcomes from CAP is important since it affects both treatment and clinical outcome. Outcome is also affected by inappropriate choice of empiric treatment, since it has been found to be an independent risk factor for early treatment failure or death [21,22]. This paper will review the factors influencing the degree of risk for poor outcome in patients with CAP and look at strategies designed to optimise therapeutic management of the condition.

Table 1 Prevalence of pathogens isolated in community-acquired pneumonia by treatment setting.

	Outpatients (%)	Hospitalised patients non-ICU (%)	ICU patients (%)
S. pneumoniae	38	27	28
M. pneumoniae	8	5	2
H. influenzae	13	6	7
C. pneumoniae	21	11	4
S. aureus	1.5	3	9
Enterobacteriaceae	0	4	9
P. aeruginosa	1	3	4
Legionella spp.	0	5	12
C. burnetii	1	4	7
Respiratory viruses	17	12	3
Unknown	50	41	45

ICU, intensive care unit.
Reproduced with permission from Welte et al. Thorax 2012 [5].

The 'at risk' patient

A number of variables are associated with increased risk of poor outcome, including the aetiology [6] and severity of the disease [23], the age of the patient [12], presence of comorbid illnesses [24], and the setting [6] in which patients are treated.

Aetiology

Although identifying the causative pathogen in CAP can help guide selection of the most appropriate antibiotic therapy, a microbiological diagnosis cannot be made in around 50% of patients [25], possibly due in part to difficulties associated with collecting valid sputum samples in elderly patients [26]. Nevertheless, a wide range of pathogens have been found to cause CAP, with the most common being *Streptococcus pneumoniae*, *Chlamydophila pneumoniae*, *Haemophilus influenzae*, *Legionella* spp., *Staphylococcus aureus* and Enterobacteriaceae [5]; similar bacteriological patterns occur in younger and older patients [26]. Of these pathogens, *S. pneumoniae* is the most frequently isolated, both in outpatients and hospitalised patients, including those in the intensive care unit (ICU) [5,27] (Table 1). *S. pneumoniae* is also reported to be common in patients with severe sepsis [28] and has been found to trigger bacteraemia and sepsis in mouse lung infection models [29]. *H. influenzae* is the second most frequently isolated pathogen, being found in 5—14% of elderly CAP patients [5,26,30]. Although *S. aureus* is a relatively uncommon cause of CAP, outcomes for patients with *S. aureus* CAP are poor [31]. Furthermore, methicillin-resistant *S. aureus* (MRSA) is becoming an increasingly

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