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Initial Evaluation and Management of Severe Community-Acquired Pneumonia

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Community-acquired pneumonia (CAP) remains a common cause of morbidity and mortality. In 1998, the World Health Organization (WHO) reported >3.7 million deaths from lower respiratory tract infections (RTIs) worldwide. In Canada, pneumonia and influenza are the 6th leading cause of death overall and the leading cause of death from infectious diseases. In the United States, >1 million patients with CAP require hospitalization annually, with 10% requiring admission to the intensive care unit (ICU). In patients who are hospitalized, mortality from CAP is as high as 12% and increases to 22% if they are admitted to the ICU with severe CAP (S-CAP). For elderly ICU patients requiring mechanical ventilation, mortality increases to 55%.¹ This issue of *Critical Care Rounds* reviews the initial evaluation and management of S-CAP, with an emphasis on a comparison of CAP guidelines published by major scientific societies as they pertain to defining and assessing S-CAP, microbial etiology and investigations, and immediate management. Finally, major recent changes and developments in our perspective of S-CAP are discussed, including recombinant human activated protein C, low-dose steroid therapy, the use of management guidelines and critical pathways, and infectious control precautions. S-CAP in immunocompromised patients and in children is not specifically discussed in this review since these patients have a distinct spectrum of presentation and require unique diagnostic and therapeutic approaches.

Definition and risk stratification

A number of scientific societies have published guidelines on CAP and endorsed different predictive rules, severity indices, and definitions of S-CAP. The most scrutinized, widely disseminated, and relevant guidelines for Canadian practitioners include those published by the Canadian Infectious Diseases Society/Canadian Thoracic Society (CIDS/CTS),² the Infectious Diseases Society of America (IDSA),^{3,4} the American Thoracic Society (ATS),⁵ and the British Thoracic Society (BTS).⁶

The CIDS/CTS and the IDSA both endorse use of the pneumonia severity index (PSI). The PSI was initially proposed by Fine et al in 1997 as a systematic way of stratifying CAP and identifying those at greatest risk of adverse outcomes.⁷ The PSI stratifies patients into 5 classes (with “class 1” being the lowest-risk group and “class 5” being the highest), based on admitting clinical factors in an effort to predict 30-day mortality. Although proven to be a powerful predictor of mortality, the PSI was initially designed to identify low-risk patients who do not require hospitalization and was not specifically intended to define S-CAP or the need for ICU admission. Furthermore, the PSI encompasses 20 different variables, each with differential weighting of importance and, as a consequence, has been criticized as being too bulky and impractical for routine clinical use.

The 2001 ATS criteria for S-CAP were developed to identify patients requiring ICU management and represent a modification (based on a prospective assessment of S-CAP by Ewig et al⁸) of previous ATS criteria.⁵ This modified ATS risk assessment (hereafter referred to as the “modified 2001 ATS criteria”) defines S-CAP as the presence of 1 major criteria or 2 minor criteria. *Major criteria* were defined as septic shock or the need for mechanical ventilation, while *minor criteria* included systolic blood pressure (SBP) <90 mm Hg; multi-lobar disease; or a PaO₂/FiO₂ ratio of <250.

Alternate criteria, endorsed by the ATS in 2001 (hereafter referred to as the “alternate 2001 ATS criteria”), included 2 *additional major criteria* (an increase in the size of infiltrates by >50% within 48 hours [h] and acute renal failure defined as urine output <80 ml in 4 h or serum creatinine >2 mg/dL in the absence of chronic renal failure) and 2 *additional minor criteria* (respiratory rate >30/min and diastolic blood pressure (DBP) <60 mm Hg).

The 2001 BTS guidelines support a definition of S-CAP based on a set of core adverse prognostic features including:

- confusion
- urea >7 mmol/L
- respiratory rate >30/min
- SBP <90 mm Hg and/or
- DBP <60 mm Hg⁶



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This scoring system is referred to as the “modified BTS” or “CURB” (confusion, urea, respiratory rate, blood pressure) and defines S-CAP as the presence of 2 or more adverse prognostic features. The BTS guidelines also support the designation of S-CAP in patients with only 1 core adverse prognostic feature, based on clinical judgment, particularly if there are pre-existing adverse prognostic features (age > 50 years or coexisting disease) or additional clinical adverse prognostic features such as bilateral/multilobar involvement or hypoxemia (SaO₂ <92% or PaO₂ <60 mm Hg), regardless of FiO₂.

To be clinically relevant and applicable, any definition of S-CAP must show validity in predicting meaningful outcomes such as ICU admission or mortality. Toward this end, Angus et al⁹ retrospectively reviewed 1339 patients from the Pneumonia Patient Outcomes Research Team (PORT) cohort that included 170 ICU admissions. In this cohort, the modified ATS criteria achieved a sensitivity of 70.7% and a specificity of 72.4% in predicting the need for ICU admission. These authors also assessed the validity of the PSI and reported risk class IV and V to have a sensitivity of 72.9% and a specificity of 53.4% in predicting the need for ICU admission. For prediction of mortality, the revised ATS criteria had a sensitivity and specificity of 39.6% and 67.6%, respectively, while the PSI had a sensitivity of 94.4% and a specificity of 53.2%. From these results, Angus concluded that the revised ATS criteria was the best discriminator of the need for ICU admission, while the PSI was the best predictor of death, although neither criteria were particularly good since both showed positive predictive values <30% for ICU admission and mortality. In an attempt to prospectively validate the modified ATS criteria, Ewig and colleagues¹⁰ studied 696 consecutive patients admitted with CAP (116 were admitted to the ICU). In predicting admission to the ICU, the modified ATS rules achieved a sensitivity of 69% and a specificity of 98%.

To validate the modified BTS severity rule, Lim et al¹¹ prospectively studied 267 adults admitted to one hospital with CAP over a 12-month period. They found that the modified BTS severity rule was 78% sensitive and 68% specific at predicting death (30-day mortality) with a negative predictive value of 95%. Furthermore, the number of core adverse prognostic features present correlated with mortality (2.7% if no core features were present, 8% if 1 core feature was present, 23% with 2, 33% with 3, and 83% with all 4 core features).

Lim et al¹² subsequently expanded the modified BTS into a 6-point scoring system called the “CURB-65” in an attempt to further stratify patients with CAP beyond the CURB system, which only delineates severe vs non-severe categories. The CURB-65 was derived and validated using combined data from 3 prospective studies of CAP (total 1068 patients) using a primary outcome measure of 30-day mortality. The new scoring system included all 4 features present in CURB, with the addition of age >65 years; hence, a 6-point score ranging from “0” to “5.” They proposed 3 categories (score 0-1 = low risk of mortality (<2%); score 2 = intermediate risk (9%), and score >2 = high risk (>19%). They suggested that this stratification system supported different management options. Although the CURB-65 may be advantageous when assessing nonsevere CAP, it does not offer an advantage over the CURB definition of S-CAP or need for ICU admission. Furthermore, CURB-65 has not yet been prospectively tested.

In conclusion, although these are valuable tools in the assessment of patients with CAP, none of the definitions or severity indices are sufficiently powerful to supplant clinical judgment and, therefore, should be viewed as adjuncts in the evaluation of individual patients. In particular, these clinical tools are not sensitive enough to predict the need for ICU admission and should not be used as the sole method of evaluation in sick patients.

Microbial etiology

S-CAP has a spectrum and prevalence of etiological agents that is distinct from less severe CAP. *Streptococcus pneumoniae* (both penicillin-sensitive and -resistant strains) has repeatedly been shown to be the most common causative organism, followed by – depending on the epidemiologic setting – Gram-negative enteric bacteria (GNEB), *Hemophilus influenzae*, atypical pathogens, *Legionella* sp., *Pseudomonas* sp., and *Staphylococcus aureus*.¹⁹

In 1999, Ruiz and colleagues reported a prospective study of 395 consecutive patients with CAP in Barcelona, Spain.¹⁴ In this study, pneumonia requiring ICU care (64 patients) was independently associated with identification of *S. pneumoniae* (odds ratio [OR] 2.5; 95% confidence interval [CI], 1.3 to 4.7), as well as GNEB, and *P. aeruginosa* (OR 2.5; 95% CI, 0.99 to 6.5). The same group published a case control study of 91 patients admitted to the ICU with S-CAP who were matched to patients with CAP not requiring ICU. Again, *S. pneumoniae* was the most frequent organism (24%) (48% of strains were drug-resistant), followed by atypical pathogens (17%; ie, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *C. burnetii*); GNEB (6%), and *P. aeruginosa* (5%).¹⁵ Of note, a microbial origin was only identified in 53% of patients with S-CAP, while 16 patients had >1 organism identified.

The microbiology of S-CAP in North America appears similar. In a prospective study of 104 elderly (> 75-years-old) with S-CAP from 2 hospitals in Buffalo, New York, the most commonly identified pathogens were *S. pneumoniae* 14%, GNEB (14%), *Legionella* (9%), *H. influenzae* (7%), and *S. aureus* (7%).¹⁶

An appreciation of the common pathogens associated with S-CAP is necessary when contemplating empiric therapy and, in that regard, a number of important considerations must be borne in mind.

- First, the pathogenic spectrum and prevalence must be tailored to different geographic and demographic settings.
- Second, mixed infections must always be considered, particularly when narrowing antibiotic coverage (even if only a single organism has been isolated).
- Third, *Pseudomonas* should be considered in those with structural damage to the respiratory tract, prolonged broad spectrum antibiotic therapy, malnutrition, HIV, and immunosuppression since these patients are more susceptible to *Pseudomonas* respiratory infections.¹⁷
- Fourth, in many cases, microbial investigations will not identify a causative agent and, therefore, modification or narrowing of the initial antimicrobial choice may not be possible.
- Finally, viral respiratory infections caused by influenza, respiratory syncytial virus, and parainfluenza, can all cause S-CAP, particularly in the elderly and immunocompromised.

Microbial investigations

Initial investigative procedures aimed at identifying causative organisms may be helpful in directing antimicrobial therapy and establishing epidemiological trends. However, noninvasive investigations (eg, sputum Gram stain and culture, blood culture, and serology) all have limitations in terms of validity and diagnostic yield, while invasive procedures carry a risk of iatrogenic morbidity and mortality. Although useful for epidemiological studies and reporting, it should be noted that, with the exception of blood cultures for bacteremic pneumococcal infections, all microbial investigations must be undertaken with the realization that no study to date has demonstrated an improvement in patient outcome with pathogen identification.

The 2000 CIDS/CTS guidelines recommend only sputum Gram stain and culture, blood cultures, and the *Legionella* urinary antigen test as part of the routine management of S-CAP.² These guidelines do not endorse any routine serological testing as they are not generally helpful in the acute setting.

The 2001 ATS guidelines also recommend 2 sets of blood cultures, with sputum Gram stain and cultures recommended only if a drug-resistant pathogen or an organism not covered by usual empiric therapy is suspected.⁵ Furthermore, these guidelines suggest that sputum samples should only be used to broaden, not narrow, antibiotic coverage. As with the Canadian guidelines, no routine serological testing is recommended. *Legionella* urinary antigen testing is advised only if this organism is suspected. The ATS recommends that pleural effusions, which are either loculated or >10 mm on lateral decubitus film, be sampled, preferably before the initiation of antibiotic therapy. Invasive diagnostic techniques to obtain uncontaminated lower airway secretions are not routinely indicated as there is no evidence that establishment of a specific etiologic diagnosis improves outcome. Finally, ATS guidelines advise that bronchoscopy with protected brush or bronchoalveolar lavage (BAL) may be performed at the discretion of the clinician since this procedure carries less risk than other invasive procedures and has a reasonable sensitivity and specificity when performed correctly.

The 2003 updated CAP guidelines by the IDSA indicate that 2 pretreatment blood cultures, as well as sputum Gram stain and culture, be performed in all hospitalized patients with CAP.⁴ These guidelines also advise *Legionella* testing for hospitalized patients with enigmatic pneumonia. Specific tests for the influenza virus (by rapid antigen testing) and *C. pneumoniae* (by a 4-fold increase in IgG titer, or a single IgM titer 1:16, or isolation in tissue culture, or polymerase chain reaction (PCR) assay of respiratory secretions) are also endorsed; however, the guidelines do not define the patients or circumstances when they should be used.

The 2003 IDSA CAP update, unlike previous guidelines, incorporates the newly available Binax NOW *Streptococcus pneumoniae* urinary antigen test. In 2001, Murdoch and colleagues evaluated this rapid immunochromatographic test after performing it on 420 adults with CAP and 169 controls.¹⁸ In this study, *S. pneumoniae* antigen was detected in the urine in 16 of 20 (80%) patients with positive blood cultures for *S. pneumoniae* and in 28 of 54 (52%) patients with positive sputum cultures. The *S. pneumoniae* antigen was not detected in the urine of any control subjects by the antigen test. The 2003 IDSA guidelines endorse the use of this test only to augment standard diagnostic tests, since there is the potential advantage of rapid results. However, this test lacks the necessary sensitivity to replace blood culture as the standard of care.

Drug-resistant pneumococcus

Penicillin-resistant pneumococcus has become increasingly prevalent over the past decade. In 1996, 8.9% of *S. pneumoniae* isolates were reported to be intermediately susceptible to penicillin, while 4.4% of isolates were resistant.² More recent Canadian data from 2003 revealed the incidence of intermediate penicillin-resistant pneumococcus to be 14%, while high level resistance was reported in 6% of isolates.¹⁹ The clinical impact of pneumococcal resistance on outcome was recently reviewed by File.²¹⁻²³ The current literature suggests that penicillin remains effective for *S. pneumoniae* when the minimal inhibitory concentration (MIC) remains ≥ 2 $\mu\text{g/mL}$ and suggests that standard treatment with β -lactam antibiotics remains clinically effective against pneumococcal pneumonia when the MIC is <2 $\mu\text{g/mL}$.²¹ Currently, 3.5%-7.8% of all clinical isolates of *S. pneumoniae* have MICs ≥ 4 $\mu\text{g/mL}$. Importantly, increased mortality rates may be seen when the MIC is <2 $\mu\text{g/mL}$.

Fluoroquinolone-resistant S. pneumoniae: *S. pneumoniae* was previously universally susceptible to fluoroquinolones in Canada, however, strains resistant to this class of antibiotics have been identified at rates reported to be 0.2% to 1% in 2003.¹⁹ Although the incidence of fluoroquinolone-resistant *S. pneumoniae* is currently low, the widespread empiric use of this class of

antibiotics raises concerns that the prevalence could increase. Furthermore, clinical failures secondary to pneumococcal resistance to levofloxacin have recently been reported, indicating that this emerging resistance is clinically relevant and must be considered in patients who are not responding to treatment with fluoroquinolones.²⁴

Macrolide resistance has been steadily increasing in Canada over the last 10 years.¹⁹ Surveillance data from 2003 determined the rate of macrolide-resistant *S. pneumoniae* to be almost 16% in Canada, an increase from $<4\%$ in 1994.¹⁹ The clinical impact of macrolide resistance remains to be determined. However, macrolide resistance rates are known to be much higher among pneumococcal strains displaying penicillin-resistance,²⁵ indicating that macrolides should not be used to treat penicillin-resistant pneumococcus unless *in vitro* testing confirms macrolide susceptibility.

Empiric antimicrobial therapy

The recommendations for initial empiric antimicrobial therapy for S-CAP published by North American societies are shown in Table 1. Notably, all 3 guidelines recommend the initial use of combination therapy. The most recent recommendations (β -lactam plus an advanced macrolide or respiratory fluoroquinolone) are from the updated 2003 IDSA guidelines⁴ and are based on a lack of efficacy data to support respiratory fluoroquinolones as monotherapy in this patient population, as well as concerns of infection with resistant pathogens. The empiric use of aminoglycosides when *Pseudomonas* is a concern is endorsed by the IDSA; however, it comes with a warning that there are data to suggest that elderly patients receiving aminoglycosides may have a worse outcome. The IDSA also cautions that, in the case of pneumococcal bacteremia, the decision to continue with combination therapy or switch to a single agent must be made on an individual basis. In making this decision, it is important to bear in mind that, although not incontestable, there is growing evidence that combination therapy may be superior to monotherapy in this group of patients.²⁶ If monotherapy is chosen, penicillin G or ampicillin is recommended by the IDSA for penicillin-susceptible pathogens, while resistant strains should be treated with cefotaxime, ceftriaxone, a respiratory fluoroquinolone, or other agents, depending on sensitivity testing.

Timing of antibiotic administration

The impact of timely administration of antibiotics on outcome in S-CAP has been the subject of a number of studies. The 2001 ATS CAP guidelines recommend that antibiotic therapy be initiated within 8 hours of hospital presentation. This recommendation is based on a multicentre, retrospective, cohort study in 14,069 elderly patients with CAP published by Meehan and colleagues in 1997.²⁷ These authors reported a lower 30-day mortality associated with antibiotic administration within 8 hours (OR 0.85; 95% CI, 0.75-0.96). Similarly, a more recent retrospective study by Houck et al that assessed 18,209 medicare patients with CAP, aged >65 years and who had not received outpatient antibiotics, revealed that antibiotic administration within 4 hours was associated with reduced in-hospital mortality, 30-day mortality, and length of stay.²⁸ In contrast, a prospective, observational study of 62,000 patients with moderate-to-severe CAP (PSI Class III to V) evaluated time-to-clinical stability after stratifying patients by triage to needle time and found no significant difference between those who received antibiotics in 0 to 240 min, 241 to 480 min, or >480 min.²⁹ Further studies assessing the value of early antibiotic administration on outcomes are needed.

Respiratory pathogens and infection control

When evaluating patients from the community with respiratory failure of a potentially infectious etiology, it is important to

	Standard Therapy (<i>Pseudomonas</i> not suspected)		Antipseudomonal Therapy	
	First line	Second line	First line	Second line
CIDS/CTS 2000	IV respiratory fluoroquinolone + cefotaxime, ceftriaxone, or β -lactam- β -lactamase inhibitor	IV macrolide + cefotaxime, ceftriaxone, or β -lactam- β -lactamase inhibitor	Antipseudomonal fluoroquinolone (e.g. ciprofloxacin) + antipseudomonal β -lactam or aminoglycoside	Antipseudomonal β -lactam (ceftazidime, piperacillin- tazobactam, imipenem, or meropenem) + aminoglycoside (gentamicin, tobramycin, or amikacin) + macrolide
IDSA 2003	β -lactam (cefotaxime, ceftriaxone, ampicillin- sulbactam, or ertapenem) + advanced macrolide or a respiratory fluoroquinolone	Respiratory fluoroquinolone +/- clindamycin	Either: (1) antipseudomonal agent (piperacillin, piperacillin- tazobactam, imipenem, meropenem, or cefepime) + ciprofloxacin or (2) antipseudomonal agent + aminoglycoside + respiratory fluoroquinolone or a macrolide	Either: (1) aztreonam + levofloxacin or (2) aztreonam + moxifloxacin or gatifloxacin +/- aminoglycoside
ATS 2001	IV β -lactam (cefotaxime, ceftriaxone) + IV azithromycin or IV fluoroquinolone		Either: (1) IV antipseudomonal β -lactam (cefepime, imipenem, meropenem, piperacillin-tazobactam) + IV antipseudomonal quinolone (ciprofloxacin) or (2) IV antipseudomonal β -lactam (cefepime, imipenem, meropenem, piperacillin-tazobactam) + IV aminoglycoside + IV azithromycin or IV non-pseudomonal fluoroquinolone	

consider infection control strategies aimed at preventing transmission of respiratory pathogens.³⁰ This is particularly true for undefined febrile respiratory failure or cases that may be caused by highly infectious or virulent pathogens (eg, tuberculosis, SARS, avian influenza). Although isolation procedures are not different in the ICU compared to elsewhere in the hospital, ICU patients are more likely to undergo aerosol-generating procedures (eg, endotracheal intubation, tracheal suction, bronchoscopy, and mechanical ventilation) that can potentially increase the risk of disease transmission.

For all patient contact, standard precautions should be observed (hand washing or hand disinfection). Personal contact precautions (use of gloves, gowns, masks, and eye protection) should also be used when there is the potential for contact with blood or body fluids. Airborne precautions include isolation within a negative pressure room and the use of well-sealed N95 or greater respirators. For droplet and contact precautions, there are some data to suggest that N95 masks confer additional protection over conventional surgical masks and, therefore, it is reasonable to consider N95 masks when healthcare workers (HCWs) are involved in potential aerosol-generating procedures or if there is suspicion of a highly virulent or transmissible pathogen.³⁰ Following the SARS outbreak, "fit testing" N95 masks (to ensure that a seal has been obtained when wearing the mask) has become routine practice in many centres. It has been demonstrated that volunteers who receive fit testing have lower mucosal exposure to droplets than do those who do not receive it.³¹

The benefit of powered air-purifying respirators (PAPRs) in the ICU remains uncertain. PAPRs had previously been recommended when caring for patients with active tuberculosis and were recommended for aerosol-generating procedures during the SARS outbreak. However, there are concerns that incorrect use of PAPRs by HCWs could potentially lead to an increased risk of disease transmission and that these devices may interfere with patient care.³² PAPR use requires proper operator instruction, as well as an appreciation of the advantages and disadvantages of the system.

Critical pathways and management guidelines

A number of studies have evaluated the impact of CAP management guidelines on resource utilization, patient care, and outcomes.

- Dean et al³³ developed hospital-based CAP management guidelines based on the 1993 ATS guidelines and found a reduction in 30-day mortality among hospitalized patients in the intervention group (11% vs 14%).
- Similarly, Malone and Shaban retrospectively reviewed 330 patients from a community hospital with a diagnosis of CAP and found that nonadherence to the 1993 ATS guidelines was associated with increased in-hospital mortality (OR 4.46; 95% CI, 1.36 to 14.43).³⁴
- In a more recent study, Menendez et al also found that adherence to guidelines was protective for both mortality (OR 0.55; 95% CI, 0.3 to 0.9) and treatment failure (OR 0.65; 95% CI, 0.5 to 0.9).³⁵

- In a quality assessment analysis of CAP, Nathwani et al prospectively audited the treatment of 205 patients with CAP admitted to 2 hospitals in the UK and found that adherence to recommended antibiotic policy was associated with a reduced risk of death or readmission to hospital.³⁶

- In 2000, Marrie et al reported a large multicentre trial evaluating the effectiveness of a critical pathway for CAP.³⁷ The study found that implementation of a critical pathway reduced the use of hospital resources without causing adverse effects on outcomes.

- Addressing the value of management guidelines specifically for S-CAP, Hirani and Macfarlane compared hospital mortality among patients with S-CAP before and after guidelines were adopted and found no significant difference in overall mortality (54% before implementation and 58% after).³⁸

- Recently, Bodi et al reported a prospective multicentre study of 529 patients admitted to the ICU with S-CAP and found that nonadherence with IDSA guidelines was independently associated with death (OR 1.6).³⁹

Although the use of critical pathways and management guidelines for CAP appear to be beneficial for both patients and the healthcare system, their utility in S-CAP requires further study.

Activated protein C

In 2001, the PROtein C Worldwide Evaluation in Severe Sepsis (PROWESS) study group published a large, multicentre, phase 3, clinical trial of recombinant human activated protein C (rhAPC) in severe sepsis.⁴⁰ In this study in 1690 patients with systemic inflammation and organ failure due to acute infection, treatment with rhAPC was associated with an absolute risk reduction of 6.1% in 28-day mortality (30.8% in the placebo group and 24.7% in the rhAPC group) and a reduction in the relative risk of death of 19.4%. Also, 35.6% of the 1690 PROWESS patients were classified as S-CAP (324 in the rhAPC group and 278 in the placebo arm). In a recently published subgroup analysis of these S-CAP patients, there was an absolute risk reduction in 28-day mortality of 8.8% (22.5% and 31.3% in the rhAPC and placebo arms, respectively) and a reduction in the relative risk of death of 28%.⁴¹ Although this study possesses the inherent limitations of all subgroup analyses, the results suggest that rhAPC should be considered in patients with S-CAP who satisfy the criteria for the systemic inflammatory response syndrome and 2 organ failures.

Glucocorticoids

The use of glucocorticoids in the ICU is currently recommended for patients with septic shock who, despite adequate fluid replacement, require vasopressor therapy to maintain adequate blood pressure.⁴² A recent study by Confalonieri and colleagues suggests that there may also be a role for hydrocortisone in the treatment of patients with S-CAP.⁴³ These authors performed a multicentre, double-blind, placebo-controlled trial of intravenous hydrocortisone (200 mg bolus followed by 10 mg/h for 7 days) in patients with S-CAP, as defined by the 2001 alternate ATS criteria. By the end of the study (day 8), the hydrocortisone group had – compared to controls – a significant improvement in all primary endpoints (PaO₂/FiO₂, chest radiograph score, C-reactive protein [CRP] levels, multiple organ dysfunction syndrome score, and delayed septic shock). Hydrocortisone treatment was also associated with a significant reduction in length of hospital stay and mortality; however, these were

not the primary endpoints of the study. Two notes of cautions should accompany the interpretation of this encouraging study. First, severity of illness may have differed between the 2 groups. On entry to the study, the placebo arm displayed a significantly worse PaO₂/FiO₂ ratio, while the hydrocortisone group had higher CRP levels and higher chest radiograph scores. Second, the number of patients enrolled in the study was small (n = 48), introducing the possibility of biased estimates of treatment effect. Although not ready for general clinical application, the results of this trial are encouraging and warrant further study.

Non-invasive positive pressure ventilation

Although the current literature supports the use of noninvasive positive pressure ventilation (NPPV) as adjunctive therapy in chronic obstructive pulmonary disease (COPD) patients with acute respiratory failure,⁴⁴ and possibly selected patients with acute hypoxemic respiratory failure,⁴⁵ the utility of this therapy in S-CAP remains unproven. Confalonieri et al conducted a randomized controlled trial of NPPV in 56 patients with S-CAP⁴⁶ and found that NPPV was associated with a significant reduction in the need for endotracheal intubation (21% vs 50%) and duration of ICU stay (1.8 ± 0.7 vs 6 ± 1.8 days), but found no difference in mortality. Interpretation of this study is complicated by the inclusion of patients with COPD; a group that may uniquely benefit from NPPV for reasons that do not extend to the general S-CAP population.

In 2002, Domenighetti et al reported a prospective observational study of NPPV in non-COPD patients with either acute cardiogenic pulmonary edema or S-CAP.⁴⁷ In total, 18 patients with S-CAP were enrolled and received NPPV. Although there was a significant improvement in initial oxygenation in the NPPV group, 7 of these patients (38%) subsequently required intubation. This failure rate was identical to that reported in the subgroup of non-COPD S-CAP patients from the study by Confalonieri et al.

A similar uncontrolled study by Jolliet et al, prospectively analyzed 24 patients with S-CAP treated with NPPV and reported an intubation rate of 66%.⁴⁸ The reason for the higher intubation rate in this study (as compared to the studies by Confalonieri and Domenighetti) is unclear, but may be due to patient selection. Taken together, there is currently insufficient evidence to recommend NPPV for S-CAP patients with acute respiratory failure.

Conclusion

S-CAP remains a common clinical entity in Canada and continues to cause significant morbidity and mortality in our population. Appropriate identification and risk stratification of individuals with S-CAP, followed by suitable investigations and rational initial management, are necessary when caring for these patients. Although severity indices are valuable clinical tools, they lack the power to replace clinical judgment. An understanding of causative organisms and antimicrobial sensitivities in different patient populations and geographical locations will facilitate the selection of appropriate empiric antibiotics. There is currently insufficient evidence to recommend NPPV as part of the routine management of S-CAP patients with acute respiratory failure. Management of patients within critical pathways may facilitate optimal patient care and adherence to guidelines. New and emerging therapies for S-CAP, such as rhAPC and hydrocortisone, offer hope for improved outcomes in the future.

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