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P. Depuydt
D. Benoit
D. Vogelaers
J. Decruyenaere
D. Vandijck
G. Claeys
G. Verschraegen
S. Blot

# Systematic surveillance cultures as a tool to predict involvement of multidrug antibiotic resistant bacteria in ventilator-associated pneumonia

P. Depuydt (✉) · D. Benoit ·
J. Decruyenaere · D. Vandijck · G. Claeys ·
G. Verschraegen · S. Blot
Ghent University Hospital, Department of
Intensive Care,
De Pintelaan 185, 9000 Ghent, Belgium
e-mail: pieter.depuydt@ugent.be
Tel.: +32-9-332 2808
Fax: +32-9-332 4995

D. Vogelaers
Ghent University Hospital, Department of
Infectious Diseases,
De Pintelaan 185, 9000 Ghent, Belgium

**Abstract** *Objective:* To assess prediction of multidrug resistant (MDR) pathogens in ventilator-associated pneumonia (VAP) by systematic surveillance cultures (SC) and to assess the contribution of SC to initial antibiotic therapy. *Design:* Prospective cohort study of patients with microbiologically confirmed VAP. Comparison of actual early antibiotic coverage with three hypothetical empirical schemes. *Setting:* A 50-bed university hospital ICU. SC consisted of oral, nasal, urinary and rectal samples upon admission, 3-weekly urinary and 1-weekly oral, nasal, and rectal samples in all patients, 3-weekly tracheal aspirates in intubated patients. *Results:* MDR pathogens were found in 86 of 199 VAP episodes. Sensitivity of SC to predict MDR pathogens was 69% (tracheal SC) and 82% (all SC); specificity was 96% (tracheal) and 91% (all), respectively. Appropriate antibiotic coverage within 24 h and 48 h following MDR VAP was 77% and 89%, respectively. A carbapenem-based empirical scheme would have been equally appropriate (83% vs. 77% at 24 h; 83% vs. 89% at 48 h), but a β-lactam-fluoroquinolone empirical therapy would have been less (59% vs. 77% at 24 h; 59% vs. 89% at 48 h) as would have been β-lactam-aminoglycoside therapy (68% vs. 77% at 24 h; 68% vs. 89% at 48 h). Empirical comparators would have resulted in significantly more prescription of broad-spectrum antibiotics within the first 48 h. *Conclusions:* With MDR pathogens highly prevalent, systematic SC predicted MDR pathogens causing VAP in 69% to 82% and may have contributed to high rates of early appropriate antibiotic therapy with limited use of broad-spectrum antimicrobials.

**Keywords** Systematic surveillance cultures · Multidrug antibiotic resistance · Ventilator-associated pneumonia · Early appropriate antibiotic therapy

## Introduction

Timely administration of appropriate antimicrobials improves survival in patients with ventilator-associated pneumonia (VAP) [1–4]. VAP caused by multidrug antibiotic resistant (MDR) pathogens carries an increased risk for inappropriate empirical therapy and consequently for adverse outcome [5–9]. To maintain a high rate of initially appropriate antibiotic therapy in these infections and to limit empirical use of broad-spectrum antimicrobials where possible, clinical predictors for MDR VAP have been used for risk stratification [4, 10–12]. Microbiological results available 48–72 h following sampling may subsequently permit narrowing the spectrum of the antimicrobial therapy ("deescalation") in order to limit selection of resistant strains [13–17]. Alternative to this clinically stratified empirical prescription combined with subsequent, microbiologically guided deescalation, surveillance

cultures (SC) may provide microbiological guidance to initial antibiotic prescription [18, 19]. Previously we found that regular SC predicted 70% of bacteremic MDR microbial isolates in late-onset pneumonia at our ICU [18]. In addition, prediction of microbial cause by SC was associated with more frequently appropriate antimicrobials within 24 h of bacteremia and with better survival [20]. However, the added value of guiding initial antibiotics by SC as compared to a purely empirical broad-spectrum therapy as recommended by the updated guidelines of the American Thoracic Society was questioned [21]. In this study we assessed prospectively the prediction of MDR microbial cause of VAP by systematic SC. Additionally, we compared actual, SC-guided, initial antibiotic prescription with a hypothetical, empirical prescription based upon clinical risk stratification for MDR VAP.

## Materials and methods

### Clinical setting and design

We conducted a prospective observational cohort study between 1 April 2004 and 30 November 2006 in the 50-bed medical and surgical ICU of the 1,056-bed Ghent University Hospital. Patients aged over 16 years and intubated at least 48 h were daily evaluated for presence of pneumonia, and all consecutive microbiologically confirmed VAP episodes were retained for analysis. During the study period 267 VAP episodes (in 220 patients) were suspected and 199 episodes (in 160 patients) microbiologically confirmed (26 by BAL, 173 by endotracheal aspirate) and included for study. The median age of patients was 60 years (range 50–72), and 75% were men. Their mean Acute Physiology and Chronic Health Evaluation II score upon admission was $20.3 \pm 8.8$; 60 patients were admitted for a primary medical reason, 79 for unscheduled and 21 for scheduled surgery. ICU mortality and in-hospital mortality were 27.7% and 37.1%, respectively. The study was approved by the Ethics Committee of Ghent University Hospital.

In a first part of the study we determined sensitivity and specificity of systematic SC to predict MDR pathogens causing VAP. Therefore we considered only VAP episodes with at least one prior SC. Sensitivity was calculated by division of the number of predicted causative MDR pathogens (true predicted MDR) by the number of all causative MDR pathogens. Specificity was calculated by division of the number of MDR pathogens in SC not causing VAP (false predicted MDR) by the total number of causative pathogens subtracting this ratio from 1. In the second part of the study antibiotic therapy within the first 48 h following diagnosis of VAP was assessed in terms of rate of appropriate coverage and consumption as expressed as number of daily defined doses (DDD)

per antibiotic class. To determine the added value of SC-guided early antibiotic therapy we compared actual antibiotic prescription with three hypothetical empirical schemes (comparators).

### Microbiology

The following pathogens were considered as MDR: methicillin-resistant *Staphylococcus aureus* (MRSA), extended spectrum β-lactamase (ESBL) producing Enterobacteriaceae, MDR nonfermenting organisms such as *Acinetobacter baumannii* and *Stenotrophomonas maltophilia*, and *Pseudomonas aeruginosa* resistant for at least one of the following antipseudomonal antibiotics: ceftazidime, piperacillin, and imipenem [18, 20, 22]. During the study period no MDR outbreaks were identified at our ICU, and overall antibiotic susceptibility was constant between 2003 and 2006. In 2006 overall susceptibility of Gram-negative rods other than *P. aeruginosa* was 75%, 76%, and 95% for ceftazidime, piperacillin-tazobactam, and meropenem, respectively, 78% for fluoroquinolones and 93% for aminoglycosides. Susceptibility of *P. aeruginosa* was 78%, 79%, and 75% for ceftazidime, piperacillin-tazobactam, and meropenem, respectively, 73% for fluoroquinolones (ciprofloxacin) and 85% for aminoglycosides (amikacin). Susceptibility of *S. aureus* for methicillin was 72%.

Systematic SC consisted of oral, nasal, and rectal swabs and urinary cultures upon admission, followed by thrice weekly urinary (Monday, Wednesday, Friday) and once weekly oral, nasal, and rectal samples (Monday) in all patients, as well as thrice weekly tracheal aspirates (Monday, Wednesday, Friday) in intubated patients. SC were processed as described previously [18, 20]. All tracheal aspirates were processed semiquantitatively as a routine and quantitatively upon request. Semiquantitative scoring was derived from streaking and diluting the specimen in three segments, scored as few (+/-) for less than ten colonies, light (+), moderate (++), and heavy (+++) growth when moderate to heavy growth was observed in first, second, and third streaks, respectively. Simultaneous semiquantitative and quantitative analysis of 114 samples showed good concordance of ++ and +++ growth with more than $10^5$ CFU/ml (100%), and of ± or no growth with less than $10^4$ CFU/ml (93%). To evaluate the presence of MDR pathogens for surveillance purposes all SC (including tracheal cultures) were judged qualitatively.

### VAP definitions

VAP was considered clinically likely if a new or progressive and persistent chest radiography infiltrate was

present together with a clinical pulmonary infection score of at least six [23–26]. In our ICU bronchoalveolar lavage (BAL) is not performed systematically but is limited to patients with suspected VAP and (a) negative endotracheal aspirates, (b) infiltrates limited to upper lobes or the left lung, or (c) acute respiratory distress syndrome. BAL is performed under bronchoscopic guidance and is directed at the area with predominant infiltrates and/or the segmentar bronchi with purulent secretions.

In agreement with national guidelines [27], microbiological confirmation of clinically likely VAP required a pathogen to show ++ or +++ semiquantitative or more than $10^5$ CFU/ml quantitative growth ($> 10^4$ CFU/ml on BAL fluid) in a good quality endotracheal aspirate (with identification of more than 25 polymorphonuclear and fewer than 10 epithelial cells per low-resolution field). Additionally, clinically likely VAP with + growth on endotracheal aspirate was considered as microbiologically confirmed if Gram-staining showed predominant presence of a pathogen and antibiotic therapy had been started or changed within 72 h. VAP was considered polymicrobial if more than one pathogen grew above these thresholds. Early-onset and late-onset VAP were defined as VAP diagnosed 5 or days or fewer as opposed to more than 5 days following intubation. Antimicrobial therapy was considered appropriate if it included at least one antimicrobial drug with in vitro activity against the causative pathogen.

## Surveillance-guided antibiotic therapy and empirical comparators

In the absence of SC and in patients with negative SC the MDR risk stratification as suggested by Trouillet et al. [10] was used to guide early antibiotic prescription. If SC identified MDR pathogens, initial antibiotic therapy was SC guided. Antibiotic prescription strategy is detailed in Fig. 1. Three empirical schemes were used as hypothetical comparators: a carbapenem-based scheme and two β-lactam-based schemes (a β-lactam-fluoroquinolone and a β-lactam-aminoglycoside scheme). The carbapenem scheme reflected the recommendations of the updated American Thoracic Society (ATS) guidelines [4] and was defined as a limited spectrum β-lactam antibiotic for early-onset VAP with no prior antibiotic exposure, and of a combination of a carbapenem plus a fluoroquinolone plus a glycopeptide for VAP with risk factors for MDR pathogens. The β-lactam-fluoroquinolone and β-lactam-aminoglycoside schemes were based upon the Trouillet et al. [10] risk classification and were defined as prescription of a non-antipseudomonal β-lactam antibiotic in early-onset VAP with no prior antibiotic exposure, an antipseudomonal β-lactam antibiotic in VAP with one risk factor for MDR (late-onset VAP and prior antibiotic exposure) and a glycopeptide added to double antipseudomonal coverage in VAP with both risk factors for MDR; double antipseudomonal coverage consisted of an antipseudomonal β-lactam plus a fluoroquinolone in the β-lactam-fluoroquinolone scheme and of an antipseudomonal



**Fig. 1** Surveillance-guided prescription and empirical prescription (in the absence of surveillance cultures (*SC*) or with negative SC). [1] If previous exposure to antipseudomonal β-lactam; [2] if Gram-positive cocci on Gram-staining and (other) MRSA-colonized patient at the ICU unit; [3] if documented susceptibility on SC; [4] in the absence of septic shock; [5] if *P. aeruginosa* resistant to both β-lactam and carbapenem
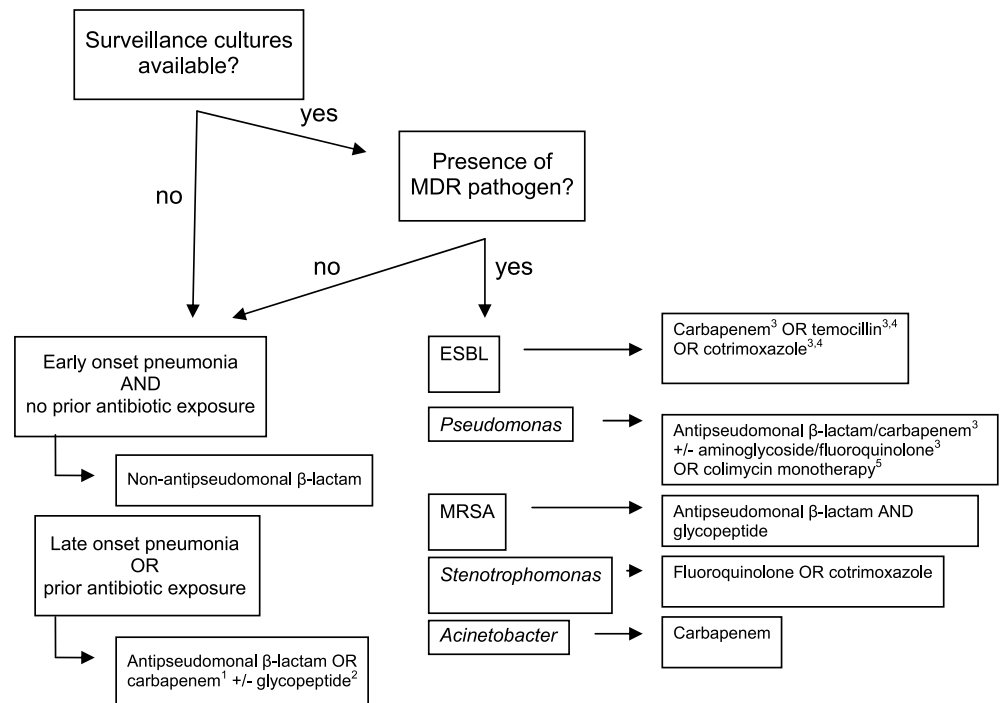
β-lactam plus an aminoglycoside in the β-lactam-aminoglycoside scheme.

## Statistics

Continuous variables are described as mean (± standard deviation) or median (interquartile range) for normal or nonnormal distribution, respectively. Categorical variables are described as absolute numbers (and percentages). For comparative tests on continuous variables the Mann–Whitney $U$ test and $t$ test were used as appropriate, depending on variable distribution. For categorical variables Pearson's $\chi^2$ test or Fisher's exact test were used as appropriate. Statistical analyses are executed with SPSS 11.0 (SPSS, Chicago, Ill., USA). All used tests were two-tailed and statistical significance was defined as $p < 0.05$.

## Results

### Microbiology of VAP and prediction by SC

VAP was monomicrobial in 170 and polymicrobial in 29. Gram staining of endotracheal aspirate showed predominant growth of a pathogen in 76%. In 86 episodes (43%) at least one MDR pathogen was identified (Table 1). In total 93 of 230 identified microbial pathogens were MDR: 13 MRSA, 45 ESBL-producing Enterobacteriaceae, 24 MDR *P. aeruginosa* and 11 MDR nonfermenters other than *P. aeruginosa*. Availability of SC and prediction of MDR by SC in the different clinical risk categories for MDR infection are detailed in Table 2. Overall sensitivity of MDR prediction by SC was 69% for tracheal SC and 82% for all SC. Specificity of MDR prediction by SC was 96% (tracheal SC) and 91% (all SC). Assuming a prevalence of 43% MDR VAP, positive predictive values of tracheal and all SC to the type of MDR pathogen in VAP were 90% and 87%, respectively, and negative predictive values of tracheal and all SC were 80% and 87%, respectively.

### Early antibiotic therapy

Within 24 h and 48 h of VAP diagnosis antimicrobial therapy was appropriate in 86% and 93% in the whole cohort, respectively, and in 77% and 89% in patients with MDR VAP. Combination antibiotic therapy was prescribed in 49 patients (25%). Appropriate antimicrobial coverage by the empirical comparators is shown in Table 3. In MDR VAP appropriate coverage by the carbapenem scheme would not have differed from actual coverage (83% vs. 77% at 24 h, $p = 0.4$; 83% vs. 89% at 48 h, $p = 0.27$), but appropriate coverage of the β-lactam-fluoroquinolone scheme would have been significantly less at both time points (59% vs. 77% at 24 h, $p = 0.01$; 59% vs. 89% at 48 h, $p < 0.001$). In contrast, appropriate coverage by the β-lactam-aminoglycoside scheme would only have been less than actual coverage at 48 h (68% vs. 77% at 24 h, $p = 0.14$; 68% vs. 89% at 48 h, $p = 0.001$). Total antibiotic prescription for 48 h following diagnosis of VAP was lower than that of empirical comparators (Table 3).

**Table 1** Microbial cause of 199 episodes of ventilator-associated pneumonia (*VAP*)[a] (*MDR*, multidrug-antibiotic resistant; *MSSA*, methicillin-susceptible *Staphylococcus aureus*; *MRSA*, methicillin-resistant *S. aureus*)

| | |
|---|---|
| **VAP episodes without MDR pathogens (*n* = 113)** | |
| Monomicrobial VAP (*n* = 103) | |
| Streptococcus pneumoniae | 4 |
| MSSA | 10 |
| Enterobacteriaceae | 42 |
| *Pseudomonas aeruginosa* | 36 |
| *Haemophilus influenzae* | 9 |
| *Proteus mirabilis* | 2 |
| Polymicrobial VAP (*n* = 10) | |
| Gram-positive and Gram-negative | |
| *Streptococcus milleri*/Enterobacteriaceae | 1 |
| MSSA/Enterobacteriaceae | 5 |
| Polymicrobial Gram-negative | |
| *P. aeruginosa* + Enterobacteriaceae | 1 |
| Other Gram-negatives | 3 |
| **VAP episodes with at least one MDR pathogen (*n* = 86)** | |
| Monomicrobial VAP (*n* = 67) | |
| MDR Enterobacteriaceae | 33 |
| MDR *P. aeruginosa* | 18 |
| MRSA | 9 |
| MDR *Stenotrophomonas maltophilia* | 4 |
| MDR *Burkholderia cepacia* | 3 |
| Polymicrobial VAP (*n* = 19)[b] | |
| Gram-positive and Gram-negative | |
| MSSA + MDR Enterobacteriaceae | 2 |
| MRSA + non-MDR *P. aeruginosa* | 2 |
| MRSA + other non-MDR Gram-negatives | 2 |
| Polymicrobial Gram-negative | |
| MDR *P. aeruginosa* + MDR Enterobacteriaceae | 4 |
| Two MDR Enterobacteriaceae | 2 |
| MDR Enterobacteriaceae + non-MDR *P. aeruginosa* | 2 |
| MDR *P. aeruginosa* + other non-MDR Gram-negatives | 2 |
| MDR *B. cepacia* + non-MDR Enterobacteriaceae | 1 |
| MDR *S. maltophilia* + MDR Enterobacteriaceae | 1 |
| MDR *S. maltophilia* + non-MDR Enterobacteriaceae | 1 |

[a] In 189 episodes pathogen growth exceeded cutoffs of ++ (semiquantitative) or $10^5$ CFU/ml (quantitative) on endotracheal aspirate or $10^4$ CFU/ml on BAL fluid (*n* = 26). In ten episodes Gram staining was positive but pathogens showed + growth on endotracheal aspirate [two *S. pneumoniae*, one MSSA, six (antibiotic susceptible) Enterobacteriaceae, one *P. aeruginosa*]; all of these patients had received new antibiotic therapy within 72 h of sampling (nine non-antipseudomonal β-lactam antibiotic because of suspected or witnessed gross aspiration, one antipseudomonal β-lactam antibiotic because of septic shock)

[b] In two polymicrobial episodes three pathogens were identified, respectively, MSSA, non-MDR *E. coli* and MDR *E. aerogenes*, and *P. aeruginosa*, non-MDR *E. coli* and MDR *E. aerogenes*. In all other polymicrobial episodes two pathogens were identified

**Table 2** Prevalence of multidrug antibiotic-resistant (*MDR*) pathogens, availability of surveillance cultures (*SC*) and prediction of MDR pathogens by SC according to risk category for MDR VAP

| | Early onset (n = 79) No prior antibiotics (n = 28) | Prior antibiotics (n = 51) | Late onset (n = 120)[a] | p[a] |
|---|---|---|---|---|
| MDR cause | 4 (15%) | 15 (29%) | 67 (56%) | < 0.001 |
| SC available at diagnosis of VAP | 1 (4%) | 36 (71%) | 114 (95%) | < 0.001 |
| MDR predicted by tracheal SC | 1 (25%) | 6 (40%) | 50 (75%) | 0.023 |
| MDR predicted by any SC | 1 (25%) | 8 (53%) | 58 (85%) | 0.36 |
| False MDR prediction by tracheal SC | 0 | 0 | 6 (5%) | 0.29 |
| False MDR prediction by any SC | 0 | 3 (8%) | 11 (10%) | 0.36 |

[a] 118 patients received prior antibiotic therapy
[b] Pearson's $\chi^2$ comparison between more than two groups

**Table 3** Appropriate coverage rates and components of actual antibiotic prescription (overall episodes and in subgroups with and without multidrug resistant, *MDR*, pathogens) in comparison with three hypothetical, empirical schemes[a]. Antibiotic components are expressed as sum of defined daily dose (*DDD*) of antibiotic classes (*naPBl*, non-antipseudomonal β-lactam antibiotic; *aPBl*, antipseudomonal β-lactam antibiotic; *Fq*, fluoroquinolone; *Ag*, aminoglycoside; *Gly*, glycopeptide; *Ca*, carbapenem; *DDD*, daily defined dose; *MDR*, multidrug resistant; *VAP*, ventilator-associated pneumonia)

| | Observed | Hypothetical Carbapenem scheme | β-lactam/ fluoroquinolone scheme | β-lactam/ aminoglycoside scheme |
|---|---|---|---|---|
| **Overall episodes (n = 199)** | | | | |
| Appropriate coverage | | | | |
| 24 h | 86% | 88% | 76%[a] | 80% |
| 48 h | 93% | 88% | 76%[a] | 80%[b] |
| Antibiotic DDD for the first 48 h | | | | |
| naPBl | 101 | 55 | 55 | 55 |
| aPBl/Ca | 201 | 342 | 342 | 342 |
| Fq | 55 | 342 | 240 | 0 |
| Ag | 8 | 0 | 0 | 240 |
| Gly | 44 | 342 | 240 | 240 |
| Other[c] | 45 | 0 | 0 | 0 |
| **Episodes with MDR (n = 86)** | | | | |
| Appropriate coverage | | | | |
| 24 h | 77% | 81% | 56%[a] | 68%[b] |
| 48 h | 89% | 81% | 56%[a] | 68%[b] |
| Antibiotic DDD for the first 48 h | | | | |
| naPBl | 25 | 8 | 8 | 8 |
| aPBl/Ca | 95 | 164 | 164 | 164 |
| Fq | 26 | 164 | 134 | 0 |
| Ag | 4 | 0 | 0 | 134 |
| Gly | 37 | 164 | 134 | 134 |
| Other[c] | 32 | 0 | 0 | 0 |
| **Episodes without MDR (n = 113)** | | | | |
| Appropriate coverage | | | | |
| 24 h | 92% | 92% | 89% | 89% |
| 48 h | 96% | 92% | 89% | 89% |
| Antibiotic DDD for the first 48 h | | | | |
| naPBl | 76 | 47 | 47 | 47 |
| aPBl/Ca | 106 | 178 | 178 | 178 |
| Fq | 29 | 178 | 106 | 0 |
| Ag | 4 | 0 | 0 | 106 |
| Gly | 7 | 178 | 106 | 106 |
| Other[3] | 13 | 0 | 0 | 0 |

[a] Appropriate antibiotic coverage of the β-lactam-fluoroquinolone scheme was significantly lower than that of actual prescription both at 24 h and 48 h ($p < 0.05$) in the overall group and in the subgroup with MDR VAP
[b] Appropriate antibiotic coverage of β-lactam-aminoglycoside scheme at 48 h was significantly lower than that of actual prescription at 48 h ($p < 0.05$) in the overall group and in the subgroup with MDR VAP; at 24 h this difference showed a trend to significance in the subgroup with MDR VAP ($p = 0.06$)
[c] Other antibiotics include trimethoprim-sulfamethoxazole and colimycin

## Discussion

In our prospective study in patients with VAP sensitivity of systematic SC to predict MDR causative pathogens (69–82%) was similar to that reported in our retrospective study in bacteremic VAP [18] but with a much higher specificity (81–96%). In a setting of high prevalence of MDR pathogens this resulted in a high positive predictive value.

Our study is to be compared with four others assessing the potential of SC in predicting microbial cause of VAP. In a prospective study of VAP following cardiac surgery Bouza et al. [26] found SC to predict only one single episode. However, only 28 episodes (of which only 8 or 9 late-onset) of VAP were analyzed, no information regarding MDR occurrence was provided, and SC were taken only once weekly in patients ventilated longer than 1 week. A second study by Hayon et al. [27] reported that 42% of 165 episodes of microbiologically confirmed VAP were predicted by prior cultures (including both SC and diagnostic cultures). Prediction increased with longer duration of mechanical ventilation (49% vs. 18% prediction of at least 15 days vs. shorter than 15 days), which the authors attributed to the higher number of available cultures preceding VAP. Similarly, prediction was significantly better if less then 72 h had elapsed between the last tracheal culture preceding VAP and the bronchoscopy performed at clinical suspicion of VAP (52% of 33 episodes vs. 28% of 69 episodes, $p < 0.03$). Systematic nasal, rectal, and urinary SC taken once weekly represented only 13% of all available cultures; no tracheal aspirates were obtained at predetermined times. In contrast to these two studies Michel et al. [19] reported 83% prediction of VAP microbial cause by routine endotracheal SC twice weekly until extubation. A fourth study, published in abstract form, found 80% prediction of MDR pathogens in VAP by tracheal SC obtained twice weekly [28]. As these "positive" surveillance studies share a higher SC sampling frequency than the "negative" studies, a sampling frequency of at least twice a week might be essential to obtain a good sensitivity.

Apart from evaluating a surveillance-guided antibiotic strategy, our study is the first report assessing the coverage rate of the updated 2005 ATS guidelines for nosocomial pneumonia [4] in an ICU setting with high prevalence of MDR. A carbapenem-fluoroquinolone-glycopeptide combination scheme would have allowed 81% early appropriate therapy in MDR VAP. Strictly applied, this scheme would have required triple combination antibiotic prescription for at least 48 h in the majority ($\pm$ 86%) of VAP episodes (including MDR and non-MDR episodes). It could be argued to use results of Gram staining to limit the use of combination therapy [29]. However, relying on Gram staining of endotracheal aspirate potentially could significantly have increased erroneous therapeutic decisions in our cohort, as Gram staining was negative in 24% of microbiologically confirmed VAP and in addition revealed only one type of pathogen in 11 episodes of polymicrobial VAP caused by Gram-positive and Gram-negative pathogens. Michel et al. [19] have reported significantly better coverage rates of their surveillance based antibiotic prescription than empirical schemes based upon the ATS guidelines of 1996. It should be noted, however, that although the 2005 update of the ATS guideline was not available at the time of publication of the Michel et al. findings, the 1996 empirical scheme may not have been an adequate comparator as late as in 2004. Moreover, in their study the empirical schemes (ATS-based or "Trouillet-based") were not detailed in terms of β-lactam or carbapenem preference or use of combination therapy with, for example, a fluoroquinolone or glycopeptide.

The different coverage rates of our three hypothetical comparators stress the importance of tailoring empirical schemes such as provided in general guidelines to the local microbial flora to obtain acceptable rates of appropriate coverage [30]. Two other studies may be mentioned here for comparison with ours. Ionas et al. [31] found 79% and 80% appropriate empirical therapy based upon the Trouillet and the 1996 ATS recommendations, respectively, in a cohort of 71 ICU patients. A 2003 study assessing the potential adequacy of selected empirical antimicrobial combinations found rates of appropriate therapy all below 70% in patients with hospital-acquired pneumonia either of early onset with specific risk factors or of late onset and prior antimicrobial therapy [32].

Some important limitations of our study should be mentioned. Firstly, although overall SC guided, part of our antibiotic prescription was empirical and was left at the discretion of the attending physician in case of no (19%) or negative SC. As our SC predicted only 69–82% of MDR cause, a strictly surveillance-based prescription may have resulted in a lower rate of appropriate therapy than actually observed as a negative SC is not an absolute argument in favor of limited spectrum empirical antibiotic therapy in the presence of risk factors for MDR. Secondly, the design of the present study does not allow testing whether outcome was positively affected by the use of SC. A randomized controlled trial comparing an SC guided antibiotic strategy to a purely empirical (e.g., deescalation) strategy is necessary to address the issue of outcome and should be preferably multicentric as resistance patterns both are highly variable between ICUs and directive of appropriate empirical schemes.

Cost resulting from the high microbiological workload is probably the most important barrier to a more widespread use of systematic SC [18] although some gains could result from limiting empirical antibiotic prescription. To contain this workload SC may be restricted to patient categories where the risk for MDR infection is highest, such as patients admitted from the ward after 48 h of hospital admission, patients referred from other

ICUs, and patients with prolonged (> 48–72 h) mechanical ventilation. Furthermore, for the purpose of guiding antibiotics in VAP it could be argued to concentrate efforts on frequent surveillance of the airways only [19, 28]. A decision whether to try systematic SC as a strategy to improve empirical prescription should finally depend on local availability of microbiological laboratory resources, endemicity and susceptibility patterns of MDR pathogens, and urgency to curtail the use of certain classes of broad-spectrum antibiotics [33–35]. Tracheal surveillance in patients ventilated for at least 72 h is probably the more cost-effective part of a systematic SC program and could be assessed in a randomized trial.

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