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Effectiveness of and obstacles to antibiotic streamlining to amoxicillin monotherapy in bacteremic pneumococcal pneumonia

Mathieu Blot [a], Diane Pivot [b], Abderrahmane Bourredjem [c], Arnaud Salmon-Rousseau [a], Claire de Curraize [d], Delphine Croisier [a], Pascal Chavanet [a], Christine Binquet [c], Lionel Piroth [a,*]

[a] Service de maladies infectieuses et tropicales, CHU, Dijon, France
[b] Service d'épidémiologie et d'hygiène hospitalière, CHU, ResAM, Dijon, France
[c] INSERM, CIC 1432, Centre d'investigation clinique (Epidémiologie clinique/essais cliniques), Dijon, France
[d] Laboratoire de bactériologie, CHU, Dijon, France

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ABSTRACT

Background: Antibiotic streamlining is pivotal to reduce the emergence of resistant bacteria. However, whether streamlining is frequently performed and safe in difficult situations, such as bacteremic pneumococcal pneumonia (BPP), has still to be assessed.
Methods: All adult patients admitted to Dijon Hospital (France) from 2005 to 2013 who had BPP without complications, and were alive on the third day were enrolled. Clinical, biological, radiological, microbiological and therapeutic data were recorded. A first analysis was conducted to assess factors associated with being on amoxicillin on the third day. A second analysis, adjusting for a propensity score, was performed to determine whether 30-day mortality was associated with streamlining to amoxicillin monotherapy.
Results: Of the 196 patients hospitalized for BPP, 161 were still alive on the third day and were included in the study. Treatment was streamlined to amoxicillin in 60 patients (37%). Factors associated with not streamlining were severe pneumonia (OR 3.11, 95%CI [1.23–7.87]) and a first-line antibiotic combination (OR 3.08, 95%CI [1.34–7.09]). By contrast, starting with amoxicillin monotherapy correlated inversely with the risk of subsequent treatment with antibiotics other than amoxicillin (OR 0.06, 95%CI [0.01–0.30]). The Cox model adjusted for the propensity-score analysis showed that streamlining to amoxicillin during BPP was not significantly associated with a higher risk of 30-day mortality (HR 0.38, 95%CI [0.08–1.87]).
Conclusions: Streamlining to amoxicillin is insufficiently implemented during BPP. This strategy is safe and potentially associated with ecological and economic benefits; therefore, it should be further encouraged, particularly when antibiotic combinations are started for severe pneumonia.

1. Introduction

The use of broad-spectrum antibiotics has significantly increased in outpatients in France [1], and is associated with the emergence of bacterial resistance. This is particularly true in severe community-acquired pneumonia (CAP), where *Streptococcus pneumoniae* (*S.p.*) remains the main causative agent [2], and even more so in hospital-acquired pneumonia (HAP), for which antibiotics with a significant ecological impact (such as cephalosporin, antipseudomonal β-lactam antibiotic, and quinolone) are increasingly used [3,4]. Antibiotic streamlining is needed to lower antibiotic pressure and thus the development of antimicrobial resistance [5]. Antibiotic streamlining generally refers to a reduction in the spectrum of administered antibiotics through the discontinuation of antibiotics or by switching to an agent with a narrower spectrum.

From this point of view, bacteremic pneumococcal pneumonia (BPP) is of particular interest. Firstly, it is more frequently observed in more severely ill patients or in the patients at higher risk of complications, thus leading to a more frequent empirical use of wide-spectrum antibiotics or combinations. Secondly, by offering the opportunity to both isolate the causative agent and assess its susceptibility to antibiotics, it provides valuable information to implement antibiotic streamlining towards narrower spectrum antibiotics, i.e., amoxicillin, which remains the treatment of reference, as the prevalence of penicillin resistance is relatively low in France and other countries [6].

* Corresponding author. Département d'Infectiologie, CHU, 14 rue Paul Gaffarel, 21079 Dijon, France.
E-mail address: lionel.piroth@chu-dijon.fr (L. Piroth).

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However, studies that focus on streamlining in BPP are scarce, and show that this strategy is not so common, being applied in 46% to 63% of patients [7–9]. This could be linked to the results of certain retrospective studies, which concluded that the use of antibiotic combinations (especially β-lactam-macrolide) could reduce mortality rates in pneumococcal pneumonia compared with monotherapy [10]. Lastly, conflicting effects of streamlining on outcome have been reported in studies in critically ill patients [7,11,12]. Nevertheless, this has to be weighed against the results of a recent meta-analysis, which indicated that antibiotic susceptibility testing (AST)-based streamlining in patients with bacteremia, severe sepsis and ventilator-acquired pneumonia was associated with a lower unadjusted mortality rate [13]. This was not observed in patients with other types of pneumonia [13]. However, there was no significant difference in mortality in the adjusted analysis and a non-significant trend towards increased mortality was found with the streamlining strategy when the analysis was restricted to only the three randomized controlled trials [13].

Thus, there is still some uncertainty about whether antibiotic streamlining is safe in pneumonia. As no new randomized controlled trials on this topic are likely to be conducted in the near future, observational studies assessing the safety of antibiotic streamlining after adjusting for confounding factors should be informative. In addition, the impact of streamlining to amoxicillin monotherapy in BPP has never been assessed.

The present study was therefore conducted to assess factors associated with not streamlining to amoxicillin monotherapy in BPP, and to determine the impact of streamlining on outcome in patients.

2. Patients and methods

2.1. Study design

All adult patients hospitalized for BPP (either community-acquired or healthcare-related) in several wards of Dijon University Hospital between January 1st 2005 and March 31st 2013 were included in a prospective cohort (French National Hospital Clinical Research Program [PHRC] 2004/37). Data were collected via standardized report forms. This cohort was completed retrospectively by adding patients hospitalized for BPP in the same hospital during the same period, who had not been included in the prospective cohort study for logistical reasons.

The study was conducted in accordance with the Declaration of Helsinki and National standards. The collection of nominative data was approved by the national authority for the protection of privacy and personal data and by the local ethics committee (Comité de protection des personnes Est I).

2.2. Inclusion and non-inclusion criteria

To be included in the present study, patients had to meet the following criteria: (1) aged over 18 years; (2) positive blood cultures for *S. pneumoniae*; and (3) diagnosed with pneumonia, defined as an acute illness (<10 days of symptoms) with the presence of a new pulmonary infiltrate on chest radiograph at the time of hospitalization, plus either a new or increased cough with or without sputum production, or an abnormal temperature (<35.6 °C or >37.8 °C), or an abnormal serum leukocyte count: i.e., leukocytosis (leukocyte count $\geq 10 \cdot 10^6$/L), left shift, or leukopenia (leukocyte count $<4 \cdot 10^6$/L).

Patients who died during the first 3 days were not included, nor were those with missing data and those for whom concomitant meningitis, endocarditis, spondylitis or arthritis was discovered during the first 3 days after hospital admission.

Healthcare-associated pneumonia (HCAP), HAP, and CAP were defined according to the guidelines of the American Thoracic Society/Infectious Diseases Society of America [4,14]. HCAP corresponded to any of the following: hospitalization for ≥2 days in the preceding 90 days; residence in a nursing home; home infusion therapy; long-term dialysis within 30 days; and home wound care. HAP was defined as pneumonia that occurred 48 hours or more after admission and that was not incubating at the time of admission.

2.3. Study variables

Demographic data, medical history, initial clinical presentation, and biological findings (first 24 hours), antibiotic treatment, microbiological culture results, and outcome were all recorded. To evaluate disease severity, clinical and biological data were collected for the first 24 hours to calculate the Pneumonia Severity Index (PSI) score as defined by Fine et al [15]. The PSI scores were classified as low (class I to III) and high (class IV to V) [15]. The following therapeutic data were recorded: mechanical ventilation and admission to an intensive care unit (ICU). Immunosuppression included human immunodeficiency virus seropositivity; daily administration of corticosteroids (at least 5 mg per day of prednisone or an equivalent drug); immunosuppressive therapy; chemotherapy for an underlying malignancy during the 6 months before hospital admission; and primary or secondary hypogammaglobulinemia, hypocomplementemia, and splenectomy [16].

The susceptibility of bacterial strains to antibiotics was assessed according to the 2016 European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints [17]. Minimal inhibitory concentrations (MICs) above 0.5 mg/L for penicillin G and amoxicillin defined non-susceptibility.

Antibiotic treatments were assessed throughout the follow-up of the patients, with special attention paid to the third and seventh days.

2.4. Judgment criterion/outcome

Streamlining was defined as either changing an initially appropriate antimicrobial therapy (or discontinuing an antimicrobial combination) to amoxicillin monotherapy (also called de-escalation), or continuing either intravenous or oral amoxicillin monotherapy, according to the microbial culture results, on the third day after the blood culture was received at the Microbiology Department.

Thirty-day mortality was reported as the proportion of patients who died within 30 days after hospitalization. Follow-up was recorded as the number of days from the date the blood sample was received at the Microbiology Department to death or to the 30-day censoring point.

2.5. Statistical analysis

Continuous variables were expressed as medians (interquartile ranges [IQR]), and categorical variables as frequencies (percentages). Continuous data were compared using the Mann–Whitney U–test, and categorical data were compared using the χ^2 test (and Fisher's exact test when appropriate). Forward stepwise logistic regression was used for the multivariate analysis, which included all the variables with $P \leq 0.250$ in the univariate analysis. The model fit was evaluated with the Hosmer-Lemeshow goodness-of-fit test.

The cumulative probability of not streamlining to amoxicillin monotherapy was compared between patients with a low and high PSI score using the Kaplan-Meier method and the log-rank test.

A propensity score, containing all variables significantly associated with the type of antibiotic treatment on day 3, was then calculated to compare 30-day mortality between patients who were streamlined to amoxicillin and those who were not. The propensity score was estimated by first using patient age and sex and then variables with $P < 0.250$ selected in the logistic regression model:

CAP and HAP, antibiotherapy during the 6 past months, chronic renal insufficiency, immunodepression, hemoglobin, HCO3- and urea levels, mechanical ventilation, *S. pneumoniae* non-susceptible to penicillin G, and PSI. By using this propensity score, all confounding variables were merged and taken into account in the statistical comparison of outcomes of the two treatment groups. The area under the receiver operating characteristic curve (AUC) was calculated to measure the performance of the propensity score.

Survival in the two groups was estimated using the Kaplan–Meier method, and the statistical significance of differences was assessed using the log-rank test. A delayed entry was used by considering the third day after blood culture as day 0 on the graph.

The independent effect of streamlining on hazard ratios (HRs) for 30-day mortality within each subgroup was estimated via a Cox model adjusted for the propensity score, and odds ratios (ORs) of short-term outcomes were obtained using logistic regression. In comparing mortality, the HR from the Cox model and its confidence interval (CI) were compared with respect to a permissible deviation of 5% for the group without reassessment of the antibiotic treatment compared with the 're-evaluation of treatment' group. This permissible deviation corresponded to the greatest loss of efficiency that could be tolerated for the group without reassessment. *P*-values of ≤0.05 were considered statistically significant in multivariate analysis. Statistical analyses were computed using Stata 11 software, IBM SPSS 19 software and Prism software (GraphPad, San Diego California, USA).

3. Results

3.1. Population studied

Among the 238 adult patients hospitalized at Dijon University Hospital with pneumococcal bacteremia from January 2005 to March 2013, 196 had a diagnosis of pneumonia with no other known infected site. Of these, 10 were excluded from the analysis because of missing data in the follow-up and 25 because of death before the third day; therefore, 161 patients were included: 102 CAP (63%), 45 HCAP (28%), and 14 HAP (9%). No patient was lost during the 30-day follow-up period. The 30-day mortality rate was 9% (15 patients). On the third day, 60 of the 161 patients (37%) were treated with amoxicillin monotherapy (whereas 101 patients were not). Among these 60 patients who were on amoxicillin monotherapy on the third day, 21 patients (35%) had received amoxicillin monotherapy empirically from the first day, and 39 (65%) underwent antibiotic de-escalation by this time. On the seventh day, 99 (63%) of the 156 patients alive were either on amoxicillin monotherapy or without antibiotic treatment.

3.2. Baseline characteristics on the first day

Baseline characteristics of the study patients are summarized in Table 1. The median age of patients at admission was 71 years (IQR 55–84); 90 patients (56%) were male, and 128 patients (80%) had a high PSI score. Distribution of the strains according to the MIC to amoxicillin and cefotaxime is described in Fig. 1. Forty-eight (30%) of the isolated strains were considered penicillin non-susceptible pneumococci (PNSP).

Among the 106 patients who received amoxicillin monotherapy over the course of treatment, the median time between initiation of the empirical antibiotic therapy and the antibiotic streamlining to amoxicillin monotherapy was 2 days (IQR 1–4). In addition, the median ratio (time spent on amoxicillin monotherapy/total time on antibiotic therapy) was 0.63 (IQR 0–0.88).

The median duration of antibiotic therapy and of the length of hospitalization did not significantly differ between patients with and those without streamlining to amoxicillin on the third day, respectively 16 (IQR 13–20) versus 15 (IQR 12–20) days ($P = 0.67$), and 13 (IQR 8–28) versus 11 (IQR 8–18) days ($P = 0.15$).

Table 1 summarizes variables with $P \leq 0.25$ in univariate analysis. In multivariate analysis, severe pneumonia (high PSI score) and an initial treatment with at least two antimicrobial treatments were associated with non-streamlining to amoxicillin. Conversely, starting with amoxicillin monotherapy was associated with continuation of this adequate treatment from the third day onwards. Hospital-acquired pneumonia tended to be associated with not streamlining to amoxicillin ($P = 0.056$). By contrast, no significant trend was observed regarding penicillin allergy, amoxicillin non-susceptible pneumococci or co-infection with a bacterium not susceptible to amoxicillin. The model fit was good according to the Hosmer and Lemeshow test ($P = 0.942$).

Survival curves showing the probability of not streamlining according to the PSI class are shown in Fig. 2. Patients with a low PSI score on the first day were more likely than patients with a high PSI score to have streamlining (or discontinuation) of the empirical antibiotherapy during the first 14 days (log rank test, $P < 0.001$).

Of the 161 patients alive on the third day, 48 (30%) were still receiving at least two distinct antibiotic therapies, even though the results of the blood culture and the susceptibility of the *S. pneumoniae* strain were available (Table 2). Among the 156 patients alive on the seventh day, 23 (11%) were still on antibiotic combination.

A pneumococcal urinary antigen test was performed in 91 patients (57%) and 67 patients (74%) had a positive result. Antibiotic streaming was more common in patients with a positive urinary antigen test (46%) than in those without (31%, $P = 0.046$).

3.3. Safety of antibiotic streamlining to amoxicillin monotherapy during BPP

The survival rate expressed by a Kaplan-Meier curve was higher for patients with antibiotic streamlining to amoxicillin monotherapy (log-rank test, $P = 0.0442$) (Fig. 3). After adjusting for the propensity score in a Cox model, antibiotic streamlining to amoxicillin monotherapy during BPP was not significantly associated with 30-day mortality (HR 0.38; 95%CI [0.08–1.87]). The AUC of the propensity score was 0.74 [0.67–0.81], which ensures that the model was accurate. With a 5% margin, the lower confidence boundary was 2.74 and remained greater than the upper confidence boundary of the confidence interval [0.08–1.87]. Finally, the results were compatible with non-inferiority.

4. Discussion

The first main result of this study is that streamlining was performed in only 37% and 63% of the cases at 3 and 7 days, respectively, despite a robust microbiological identification (with documented *S. pneumoniae* bacteremia and susceptibility) and even though amoxicillin monotherapy remains the preferential treatment for BPP, particularly in France [3]. Indeed, although the rate of PNSP reached more than 50% of the invasive isolates in France in 2001–2002, it declined to 22.7% in 2011–2012 because of the 2001 national plan to preserve the effectiveness of antibiotics, and the 2003 introduction of the 7-valent conjugate anti-pneumococcal vaccine (PCV7) in the immunization schedule for children aged under 2 years and at risk for invasive pneumococcal diseases [6,18]. Amoxicillin non-susceptible and resistant pneumococci were indeed uncommon in the present study (19% and 2%, respectively), which is consistent with that observed in France during the same period [6]. Thus, this does not explain the low incidence of streamlining to amoxicillin in the present study because outcomes in pneumococcal pneumonia are not affected by penicillin resistance, as already stated [19,20].

Table 1
Baseline demographic, clinical, biological and therapeutic findings on admission and outcome in patients with bacteremic pneumococcal pneumonia according to whether or not treatment was streamlined to amoxicillin monotherapy.

	No streamlining 101	Streamlining 60	*P*	Multivariate analysis
Demographic data				
Age, median (IQR)	73 (58–84)	70 (47–84)	0.326	
Sex (Male), n (%)	59 (58)	31 (52)	0.404	
Comorbid conditions				
CAP, n (%)	61 (60)	41 (68)	0.312	
HAP, n (%)	13 (13)	1 (2)	0.018	10.01 [0.94–106.54]
Antibiotherapy during the 6 past months, n (%)	23 (23)	4 (7)	0.008	
Immunodepression, n (%)	27 (27)	5 (8)	0.005	
Chronic renal insufficiency, n (%)	14 (14)	2 (3)	0.031	
Chronic heart disease, n (%)	28 (28)	12 (20)	0.307	
Chronic respiratory disease, n (%)	24 (24)	12 (20)	0.580	
Clinical features on the first day				
Systolic blood pressure < 90 mmHg, n (%)	19 (19)	11 (18)	0.940	
Respiratory rate ≥ 30/min, n (%)	48 (48)	20 (33)	0.078	
Altered mental status, n (%)	14 (14)	8 (13)	0.925	
Biological features on the first day				
Hemoglobin (g/dL), median (IQR)	12.4 (10.9–13.3)	12.8 (11.9–13.8)	0.037	
Leukocytes (×10E3/mm^3), median (IQR)	13 (8–18)	16 (10–21)	0.050	
Bicarbonates (mmol/L), median (IQR)	26 (23–27)	27 (24–30)	0.056	
Blood urea (mmol/L), median (IQR)	12 (7–17)	9 (6–12)	0.028	
PaO2 < 60 mmHg, n (%)	61 (60)	34 (57)	0.642	
Prognostic score				
PSI ≥ IV, n (%)	88 (87)	40 (67)	0.002	3.11 [1.23–7.87]
Radiological findings				
Multilobar infiltrates, n (%)	37 (37)	18 (30)	0.391	
Microbiological findings				
Penicillin G MIC > 0.5 mg/L, n (%)	34 (34)	14 (23)	0.166	
Amoxicillin MIC > 0.5 mg/L, n (%)	21 (21)	9 (15)	0.361	
Amoxicillin MIC > 2 mg/L, n (%)	2	1		
Infection with another bacterium not susceptible to amoxicillin, n (%)	7 (7)	1 (2)	0.260	
Treatments, first 24 h				
Amoxicillin monotherapy, n (%)	2 (2)	20 (33)	<0.0001	0.06 [0.01–0.30]
≥2 antimicrobial treatments, n (%)	51 (51)	11 (18)	<0.0001	3.08 [1.34–7.09]
Other treatments				
Mechanical ventilation, n (%)	19 (19)	5 (8)	0.071	
ICU admission, n (%)	32 (32)	12 (20)	0.108	
Outcome				
30-day mortality, n (%)	13 (13)	2 (3)	0.044	

CAP: community-acquired pneumonia; HAP: hospital-acquired pneumonia; ICU: intensive care unit; IQR: interquartile range; MIC: minimum inhibitory concentration; PSI: prognostic score index.

This relatively low rate of streamlining is in line with that reported in other countries: in the few other cohorts of bacteremic pneumonia, treatment was streamlined in 46% to 63% of cases [7–9]. In a recent Spanish cohort analyzing the management of pneumococcal CAP using a methodology similar to that used in the present study, antibiotic streamlining within the first 72 h was performed in only 11.7% of patients [21]. However, the period of inclusion in the Spanish study was wider than that in the present study (which focused on a period with stable national recommendations on the management of CAP), and used a wider definition of pneumococcal CAP (including positive antigenuria, which enables assessment of susceptibility of the pneumococcus).

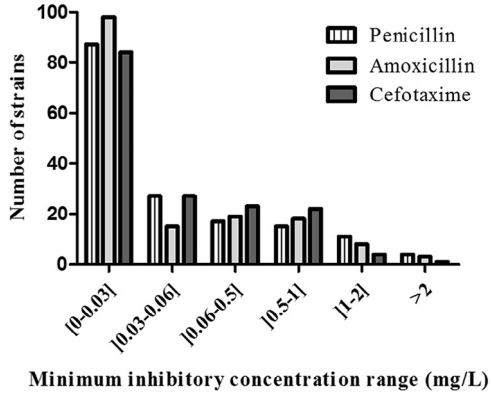

Fig. 1. Distribution of the 163 *Streptococcus pneumoniae* strains according to the minimum inhibitory concentration to penicillin, amoxicillin and cefotaxime.

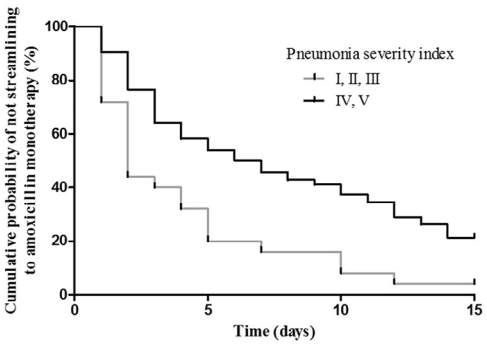

Fig. 2. Kaplan-Meier curves comparing cumulative probability of not streamlining to amoxicillin monotherapy (or discontinuation), according to the class of the Pneumonia Severity Index (log rank test, $P < 0.001$).

Table 2
Treatment regimens at different times for bacteremic pneumococcal pneumonia patients without streamlining to amoxicillin monotherapy.

Patients alive	3rd day n = 161	7th day n = 156
No streamlining to amoxicillin monotherapy	**101 (63%)**	**59 (38%)**
Monotherapy	**53 (33%)**	**34 (22%)**
Penicillin + inhibitor	26	16
Third generation cephalosporin	24	12
Fluoroquinolone	3	6
Double-therapy	**40 (25%)**	**21 (13%)**
β-lactam plus a fluoroquinolone	19	11
β-lactam plus a macrolide	13	3
β-lactam plus an aminoglycoside	7	3
β-lactam plus another	1	4
Multitherapy	**8 (5%)**	**2 (1%)**
Antibiotherapy stopped	**0**	**2 (1%)**

This could explain the rate of antibiotic streamlining, although positive antigenuria is likely to be associated with a higher likelihood of antibiotic streamlining, as indicated by the present study results. In addition, no consensual definition of antibiotic streamlining (or de-escalation) is currently available in the literature, which makes it difficult to draw direct comparisons. In most studies, the purpose of streamlining was to reduce both the spectrum of antimicrobial therapy and the selective pressure on microbiota [22].

The second main result was the observation that the implementation of antibiotic streamlining was mainly influenced by the severity and comorbidities (as assessed by the PSI score). Although most of the patients who died were excluded from the analysis because of early death, our population of BPP was characterized by high vulnerability and severe disease, as shown by the high proportion of patients with a PSI score of 4 or greater (80%). In severe patients, streamlining to a very narrow spectrum antibiotic treatment, like amoxicillin, is probably more difficult because of several issues, including prognostic uncertainty, and despite the expected reassurance provided by the isolation of a causative agent with a known susceptibility to amoxicillin. Similarly, a high PSI score was more commonly observed in patients without antibiotic streamlining in three studies [8,9,21], in addition with hypotension, tachycardia, and multilobar pneumonia in the study of Viasus et al [21]. In the present study, patients with HAP were less likely to have their antibiotic treatment streamlined. HAP frequently requires empirical broad-spectrum antibiotic therapy and probably limits streamlining to very narrow-spectrum antibiotherapy, like amoxicillin, despite robust microbiological identification. In the present study, patients with an empirical first-line combination therapy were less likely to be streamlined to amoxicillin monotherapy. That being said, in severe pneumococcal pneumonia, a macrolide-based antibiotic combination has been suggested to improve survival in retrospective studies [10] and in a matched case-control study of two prospectively recorded cohorts in Europe [23], but not in other studies [24]. The immunomodulatory properties of macrolides, the coverage of unrecognized co-infections with atypical pathogens and its non-ribosomal anti-pneumococcal activity, such as the impairment of epithelial adherence, are thought to explain the lower mortality [25].

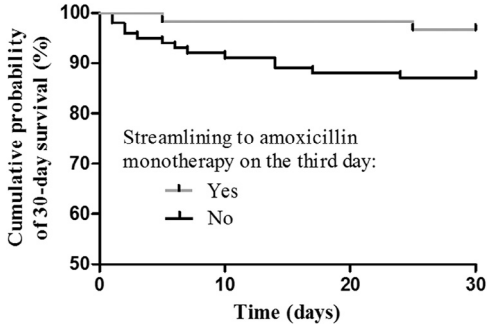

Fig. 3. Kaplan-Meier estimate for 30-day survival according to the therapeutic strategy (amoxicillin monotherapy on the third day) during bacteremic pneumococcal pneumonia. Day 0 on the graph corresponds to the third day after blood culture. There was a significant difference in 30-day mortality between the two groups (log rank test, $P = 0.0442$).

By contrast with these data, our third main finding was that streamlining to amoxicillin monotherapy on the third day in BPP was not associated with an increased risk of 30-day mortality, whatever the comorbidities, the disease severity and the empirical first-line antibiotic therapy. The lower mortality associated with streamlining to amoxicillin may be explained by the fact that narrowing the antibiotic spectrum is easier and more common in less severely ill patients. However, the use of a propensity score enabled us to adjust mortality for the main confounding variables contributing to severity. These findings are in accordance with the only two other studies on pneumococcal pneumonia dealing with antibiotic streamlining. Carugati et al found no association between streamlining and 30-day mortality among bacteremic patients with CAP after adjustment for confounders [9]. Similarly, Cremers et al showed that streamlining in pneumococcal bacteremia cases was safe, in terms of in-hospital mortality, irrespective of patient characteristics, disease severity or the empirical treatment regimen (adjusted OR 0.45, 95%CI [0.18–1.11]) [8]. When considering only pneumonia, they found a significantly reduced risk of mortality in patients with streamlining (adjusted OR 0.35, 95%CI [0.12–0.99]) [8]. An increasing amount of similar evidence has been found in ICU-acquired pneumonia [26] and ventilator-associated pneumonia [12,27,28]. The homogeneity of our study population supports streamlining to amoxicillin quite certainly in BPP, but also probably in non-bacteremic pneumococcal pneumonia, which is less severe.

A rational use of antibiotics is essential to prevent the emergence of multidrug resistant bacteria, which can lead to a therapeutic impasse. Although the emergence of resistance was rarely compared in evaluations of streamlining in pneumonia, as in the present study, one study reported a less frequent occurrence of extended spectrum beta-lactamases in the streamlined group [29]. A streamlining strategy is therefore naturally advocated as a key element in better antibiotic usage. However, we cannot exclude the possibility that we missed some patients with genuine BPP, either because blood sampling was not done or because effective antibiotic treatment was started before the blood samples were taken. The single-center nature of the study and the retrospectively collected data are also limitations. This was an observational cohort study, not a blind comparative one and it lacked a control group to show the magnitude of changes in antibiotic use resulting from the implementation of streamlined therapy. Also, there is still no universal definition of antibiotic streamlining (or de-escalation), and comparisons with other studies thus remain difficult. Patients who received amoxicillin monotherapy empirically were included in the present study. A sensitivity analysis was performed after excluding the 22 patients who received amoxicillin empirically, and showed similar results.

In conclusion, our findings indicate that streamlining to amoxicillin monotherapy on the third day is not associated with adverse outcomes in the BPP setting. Efforts must be made to implement this strategy, particularly in severe and hospital-acquired pneumonia, or when a first-line antibiotic combination has been started. Randomized clinical trials are warranted to further explore these findings.

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Competing interests: None declared.

Ethical approval: The collection of nominative data was approved by the national authority for the protection of privacy and personal data and by the local ethics committee (Comité de protection des personnes Est I).

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