Journal of Antimicrobial Chemotherapy (2009) **64**, 1307–1315
doi:10.1093/jac/dkp367
Advance Access publication 16 October 2009

JAC

Non-compliance with recommendations for the practice of antibiotic prophylaxis and risk of surgical site infection: results of a multilevel analysis from the INCISO Surveillance Network

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Received 15 July 2009; returned 10 September 2009; revised 14 September 2009; accepted 20 September 2009

***Objectives*: The aim of this study was to determine which surgical antibiotic prophylaxis (SAP) practices alter surgical site infection (SSI) risk.**

***Methods*: Data were collected during a 7 year surveillance period (2001–07) from volunteer surgery wards participating in the INCISO Surveillance Network in Northern France. Main SAP practices, i.e. antibiotic choice, timing of first dose and total SAP duration, were evaluated and compliance checked based on French recommendations. The study focused on selected procedures in digestive, orthopaedic, gynaecological and cardiovascular surgery, for which standard SAP is recommended. Multilevel logistic regression analysis (a two-level random effect model) was carried out to identify SAP-, patient- and procedure-specific factors associated with SSI.**

***Results*: Of 8029 patients who underwent the selected surgeries, 91.3% received SAP and 2.5% developed SSI. Among those receiving SAP, 83.3% received appropriate antibiotic agents and 76.6% had an optimal timing of administration. SAP duration was considered to be appropriate in 35.0%, too long (SAP unnecessarily prolonged) in 45.2% and too short (lack of intra-operative redosing when recommended) in 19.8%. In the multivariate analysis, a too-short SAP duration remained the only inappropriate practice associated with higher SSI risk (odds ratio = 1.8, 95% confidence interval: 1.14–2.81), after adjustment for surgery procedure group, the National Nosocomial Infections Surveillance System risk index, age and infection risk variability among hospitals. No significant relationships were observed between SSI and the other SAP parameters.**

***Conclusions*: A too-short SAP duration was the most important SAP malpractice associated with an increased risk of SSI. Information directed at practitioners should be reinforced based on standard recommendations.**

Keywords: surgical antibiotic prophylaxis, practice assessment, multilevel logistic regression analysis, France

Introduction

Surgical site infections (SSIs) are the most common type of nosocomial infection acquired by surgical patients.[1–3] SSIs are the third cause of nosocomial infections in France, accounting for up to 14% of all nosocomial infections in 2006.[4] These infections are a substantial burden in terms of healthcare cost and post-operative morbidity and mortality.[5,6] Since 1960, substantial research has demonstrated the effectiveness of antimicrobial prophylaxis to reduce the risk of post-operative infections for many procedures in parallel with hygiene control measures.[7–9] Likewise, numerous guidelines for optimal use of prophylactic antibiotics have been published in recent years.[10–12] Henceforth, antibiotic prophylaxis is indicated clearly for most clean-contaminated surgical wounds and some clean surgical wounds, such as vascular prostheses and orthopaedic implants.

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Consensus guidelines[10–12] state that adequate prophylaxis requires: (i) antimicrobial agents with targeted spectra of activity against organisms likely to be encountered in the particular surgical field; (ii) timely pre-operative administration of the antibiotics; (iii) bactericidal concentrations of the drugs in serum and tissues during the entire time that the incision is open; and (iv) a duration of up to 24 h following surgery. However, despite the existence of these guidelines, several studies have shown that compliance with these practices is not optimal.[13–15] The widespread abuse of prophylactic antibiotics is pervasive, harmful for patients and increases financial costs.[16] Prolonging antibiotic prophylaxis beyond 24 h not only fails to improve SSI rates, but could also favour the emergence of multidrug-resistant pathogens such as methicillin-resistant *Staphylococcus aureus* and *Clostridium difficile*.[17–19] Furthermore, inappropriate timing of administration leads to decreased efficacy.[20]

To address the issue of whether inappropriate surgical antibiotic prophylaxis (SAP) increases the risk of SSI, we conducted a study based on data collected by the surveillance network of SSI incidence in Northern France (INCISO Network). The aim of this study was to determine which SAP practice parameters (antibiotic choice, timing of first dose and total duration of prophylaxis) alter SSI risk in patients for whom SAP was indicated and compliance assessed, and to estimate the individual contribution of each SAP parameter to the SSI risk.

Methods

The INCISO surveillance system is a regional network of participating volunteer surgery wards in Northern France that was set up in 1997. This network, coordinated by the regional centre for nosocomial infection control in Northern France (C-CLIN Paris Nord), has been widely described elsewhere.[5,21] Since 1998, a yearly 3 month survey has been proposed to all volunteer surgical wards between January and March according to a protocol established by the coordinating centre. Each participating ward had to enrol the first 200 consecutive patients who underwent a surgical procedure for a 30 day post-operative follow-up. For each patient, the surgical team, helped by infection control practitioners, completed a standardized form with two sections for pre-operative and post-operative follow-up data. The form was stapled to the medical record at inclusion and a copy was sent to the infection control practitioner for follow-up. The overall items collected in the form were SSI risk factors such as age, pre-operative hospital stay, time of surgical incision and skin closure, type of surgery, American Society of Anesthesiologists (ASA) score,[22] wound class according to Altemeier classification,[23] emergency conditions, whether video surgery or multiple procedures were performed, length of post-operative stay and SSI occurrence during in- and out-hospital stay.

All patients should be followed up to 30 days after operation for SSI identification. If they were discharged before day 30, they were given an appointment by the surgeon for a post-discharge visit. The surgeon was responsible for diagnosing each SSI according to standard criteria,[24] whether at in- or out-patient hospital visit. Infection control practitioners had to collect clinical and bacteriological information for SSI identification and to check whether the surgeon took into account available information for infection diagnosis. All data were transmitted to the regional coordinating centre at the end of each surveillance period for global analysis. The National Nosocomial Infections Surveillance (NNIS) System risk index was calculated based on the 75th percentile of operation length described previously.[25] A management report was edited yearly displaying the overall results of the data network to all participant wards.

Since 2000, an annual evaluation of SAP practices has been proposed to all volunteer surgical wards participating in the INCISO Network. Thus, a standardized form for SAP data was completed for patients aged $\geq$15 years. Data collected in the SAP form provided information on whether antibiotics were used for treatment or SAP, as well as a detailed description of each SAP course related to route, dosage, administration time of all doses, time of discontinuation, names of antibiotics administered and total duration of prophylaxis.

Our study was limited to groups of surgical procedures for which standard SAP is recommended. Thus, data focused on selected digestive, orthopaedic, gynaecological and cardiovascular surgery, collected during a 7 year surveillance period (2001–07). The digestive group included appendectomy (excluding perforated appendix), small bowel surgery and colorectal surgery, the orthopaedic group included knee and hip prosthesis surgery, the gynaecology group included hysterectomy (vaginal or abdominal) and breast surgery (excluding lumpectomy) and the cardiovascular group included vascular surgery (lower limb arteries, thoracic and abdominal aorta) and cardiac surgery (open/closed heart surgery, heart valve surgery and coronary artery bypass surgery). Since wound contamination class 3 (contaminated) and 4 (dirty) interventions often required antibiotic therapy, only surgical procedures that belonged to wound contamination class 1 (clean) or 2 (clean-contaminated) were included.

Compliance with the main SAP practices, i.e. antibiotic choice, timing of first dose and total duration of prophylaxis, was assessed based on the standard recommendations of the French Society of Anesthesia and Intensive Care (SFAR) 1999 update,[11] with minor modifications limiting the duration of SAP in orthopaedic and cardiovascular surgery up to 24 h.[12] SAP compliance was defined for each SAP practice parameter and they were considered independently of each other. Thus, for antibiotic choice, compliance was stated if the antimicrobial agents used were those recommended by the SFAR. For the timing of first dose, compliance was stated if injection occurred within 60 min before incision (90 min for vancomycin). Regarding total duration of prophylaxis, compliance was stated in the following circumstances: (i) if a single dose was given for patients undergoing digestive and gynaecological surgery or when vancomycin was used; (ii) if additional intra-operative doses were re-injected when intervention lasted more than twice the half-life of the antibiotic and until the wound was closed, even if non-compliant antibiotics were used (Table 1); and (iii) if post-operative doses, not exceeding 24 h, were re-injected only for the cardiovascular and orthopaedic surgery groups.

Analysis focused only on patients for whom SAP was documented. Patients who did not receive SAP were excluded. All variables were considered as categorical: age was divided into 10 year intervals from 40 to 60 years; duration of surgery was divided into two classes according to the 75th percentile of surgical duration ($>$p75 yes or no); and pre-operative hospital stay was divided into two classes consistent with pre-operative stay $>$48 h yes or no. For each SAP practice parameter variable, the reference class was that defined as compliant. Non-compliant SAP was categorized for the timing of first dose (too-early administration: $>$60 min before incision or $>$90 min if vancomycin was used; too-late administration: after incision) and for the total duration of prophylaxis (too-short duration: lack of intra-operative redosing despite the fact that it is recommended; too-long duration: unnecessary re-injections or post-operative doses $>$24 h). Univariate analysis was performed

Table 1. Indications of intra-operative redosing according to the antibiotic used for SAP by procedure

Surgical procedure group	Antibiotic	Recommended intra-operative redosing[a]
Digestive: appendectomy (excluding perforated appendix), small bowel surgery and colorectal surgery	cefotetan	if procedure takes >3 h
	cefoxitin	if procedure takes >2 h
	amoxicillin/clavulanate	if procedure takes >2 h
	metronidazole + gentamicin[b]	no
Orthopaedic: knee and hip prosthesis surgery	cefazolin	if procedure takes >4 h
	cefamandole or cefuroxime	if procedure takes >2 h
	vancomycin[b]	no
Gynaecology: vaginal or abdominal hysterectomy and breast surgery (excluding lumpectomy)	cefazolin	if procedure takes >4 h
	clindamycin + gentamicin[b]	yes, for clindamycin if procedure takes >4 h
Cardiovascular: vascular surgery (lower limb arteries, thoracic and abdominal aorta) and cardiac surgery (open/closed heart surgery, heart valve surgery and coronary artery bypass surgery)	cefazolin	repeated doses at 4 h intervals until the wound is closed
	cefamandole or cefuroxime	repeated doses every 2 h until the wound is closed
	vancomycin[b]	no

[a]Based on recommendations of the SFAR.[11] In general, SFAR recommendations stated that additional antimicrobial doses should be provided intra-operatively if intervention lasted more than twice the half-life of the antibiotic.
[b]When allergic to β-lactam antibiotics.

using the Pearson χ^2 test to screen potential risk factors for SSI. Multivariate analysis was achieved by multilevel logistic regression analyses, with surgical procedures clustered within hospitals, using the GLLAMM software that runs in the statistical package STATA (Stata Corporation, College Station, TX, USA). A two-level random effect model was estimated.[26] Odds ratios (ORs) and their 95% confidence intervals (95% CIs) are reported, as well as hospital-level (level 2) variances and standard errors, and goodness-of-fit statistics based on −2 log likelihood ratio test (−2LL). The random effect model applied in this analysis allowed adjustment of the risk estimates for random variation between hospitals. This model is basically a logistic regression model, supplemented with an extra term in the equation for the random effects associated with differences in infection risk between hospitals. Ordinary logistic regression models do not take into account inter-hospital variability and thus they might overestimate the contribution of patient- and prophylaxis-related factors. Variables for which $P \leq 0.10$ in univariate analysis were included in the multivariate model. The final model was computed with a manual stepwise backwards elimination. Variables remained in the multivariate model if the likelihood ratio test was significant ($P < 0.05$). All computations were performed using STATA statistical software, release 10.1 (Stata Corporation).

Results

A total of 8029 surgical patients were chosen from 302 wards belonging to 149 hospitals according to the criteria defined above. Overall, 7330 (91.3%) patients were finally analysed, and 699 (8.7%) were excluded from the study as they did not receive SAP but had an indication. As shown in Table 2, the distribution by procedure groups was as follows: digestive, 23.6%; gynaecology, 13.0%; orthopaedic, 48.5%; and cardiovascular, 14.9%. The study population was predominantly female (60.8%), with a median age of 64.2 years, ASA score <3 (74.1%), operated within the standard operative time (80.0%), under elective surgery (91.9%) and pre-operative hospital stay ≤48 h (91.1%). A total of 184 SSIs were diagnosed, 105 (57.1%) during the hospital stay. The median time between surgery and SSI diagnosis was 11 days (interquartile range: 7–17 days). SSI was deep or organ/space in 34.8% and required re-operation in 25.6%. The overall SSI incidence rate was 2.5% and varied significantly according to surgical procedure, age, NNIS System risk index, ASA score, wound contamination class, duration of surgery, multiple procedures performed and a long pre-operative hospital stay (Table 2).

The compliance with SAP practices varied according to procedure group (Table 3). Overall, compliance rates were rather high for antibiotic choice (83.3%) and timing of first dose (76.6%), but poorer for total duration of SAP (35%), since 45% had a too-long SAP duration. The choice and timing of SAP administration were highly compliant (>80%) in the orthopaedic group as compared with the other procedure groups. Conversely, the compliance rate with total SAP duration was poorer in this group (11.2%). A total of 1417 (19.4%) procedures received SAP in complete compliance, 4074 (55.8%) had two SAP practice parameters compliant, 1678 (23.0%) had one SAP parameter compliant and 131 (1.8%) procedures received SAP in complete non-compliance. Regarding the antibiotic choice, the types of antibiotic that were non-compliant varied among the four surgical groups. For digestive procedures, the most frequent non-compliant antibiotics were first-generation

Table 2. Incidence of SSI, risk factors and SAP, $N=7330$ surgical procedures

Variable	No. of procedures	No. of SSIs (%)	P[a]
Surgical procedure ($N=7330$)			
digestive	1730	96 (5.5)	**<0.0001**
gynaecology	956	26 (2.7)	
orthopaedic	3555	21 (0.6)	
cardiovascular	1089	41 (3.8)	
Female gender ($N=7329$)			
yes	4459	102 (2.3)	0.13
no	2870	82 (2.9)	
Age by class in years ($N=7330$)			
≤40	684	9 (1.3)	**0.02**
41–50	1357	47 (3.5)	
51–60	1120	32 (2.9)	
>60	4169	96 (2.3)	
NNIS System risk index[b] ($N=7164$)			
0	4206	67 (1.6)	**<0.0001**
1	2600	85 (3.3)	
2	358	31 (8.7)	
ASA score[c] ($N=7318$)			
1	1880	34 (1.8)	**<0.0001**
2	3543	71 (2.0)	
≥3	1895	79 (4.2)	
Wound contamination class ($N=7330$)			
1 (clean)	4984	67 (1.3)	**<0.0001**
2 (clean-contaminated)	2346	117 (5.0)	
Duration of surgery >p75 ($N=7176$)			
yes	1437	68 (4.7)	**<0.0001**
no	5739	115 (2.0)	
Emergency circumstance ($N=7316$)			
yes	595	20 (3.4)	0.16
no	6721	163 (2.4)	
Multiple procedures performed ($N=7304$)			
yes	1006	47 (4.7)	**<0.0001**
no	6298	137 (2.2)	
Pre-operative hospital stay >48 h ($N=7326$)			
yes	655	31 (4.7)	**<0.0001**
no	6671	152 (2.3)	
Antibiotic choice for SAP[d] ($N=7330$)			
compliant	6106	130 (2.1)	**<0.0001**
non-compliant	1224	54 (4.4)	
Timing of first dose[e] ($N=7287$)			
compliant	5581	137 (2.5)	0.87
too early	985	27 (2.7)	
too late	721	18 (2.5)	

Continued

Table 2. *Continued*

Variable	No. of procedures	No. of SSIs (%)	P^a
Total duration of prophylaxis[f] ($N=6821$)			
compliant	2390	73 (3.1)	**0.03**
too short	1346	40 (3.0)	
too long	3085	62 (2.0)	

[a]χ^2 test.
[b]Includes the following elements: ASA score, wound contamination class and duration of surgery.
[c]1, healthy; 2, mild systemic disorder; ≥3, severe systemic disorder.
[d]Non-compliance was stated if the antibiotics used for prophylaxis were those not recommended in the SFAR recommendations.[11]
[e]Non-compliance was categorized as: too-early administration, >60 min before incision or >90 min if vancomycin was used; and too-late administration, after incision.
[f]Non-compliance was categorized as: too-short duration, lack of intra-operative redosing despite the fact that it is recommended; and too-long duration, unnecessary re-injections or post-operative doses >24 h.

Table 3. Compliance of SAP according to standard French recommendations by surgical group, $N=7330$ surgery procedures

Practice	Digestive ($N=1730$) *n* (%)	Gynaecology ($N=956$) *n* (%)	Orthopaedic ($N=3555$) *n* (%)	Cardiovascular ($N=1089$) *n* (%)	Overall ($N=7330$) *n* (%)
Antibiotic choice[a]					
compliant	1195 (69.1)	571 (59.7)	3335 (93.8)	1005 (92.3)	6106 (83.3)
non-compliant	535 (30.9)	385 (40.3)	220 (6.2)	84 (7.7)	1224 (16.7)
Timing of first dose[b]					
compliant	1321 (76.9)	779 (82.0)	2873 (81.3)	608 (56.0)	5581 (76.6)
too early	78 (4.5)	44 (4.6)	458 (13.0)	405 (37.3)	985 (13.5)
too late	319 (18.6)	127 (13.4)	202 (5.7)	73 (6.7)	721 (9.9)
Total duration of prophylaxis[c]					
compliant	876 (54.7)	670 (83.8)	377 (11.2)	467 (44.7)	2390 (35.0)
too short	248 (15.5)	1 (0.1)	1021 (30.2)	76 (7.3)	1346 (19.8)
too long	478 (29.8)	129 (16.1)	1977 (58.6)	501 (48.0)	3085 (45.2)

[a]Non-compliance was stated if the antibiotics used for prophylaxis were those not recommended in the SFAR recommendations.[11]
[b]Non-compliance was categorized as: too-early administration, >60 min before incision or >90 min if vancomycin was used; and too-late administration, after incision.
[c]Non-compliance was categorized as: too-short duration, lack of intra-operative redosing despite the fact that it is recommended; and too-long duration, unnecessary re-injections or post-operative doses >24 h.

cephalosporins (8.4%), third-generation cephalosporins (5.2%), aminopenicillins without β-lactam inhibitors (4.0%), nitroimidazoles without gentamicin (3.6%) and other non-specified antibiotics (4.5%). For gynaecology procedures, the most frequent non-compliant antibiotics were cephamycins (12.0%), amoxicillin/clavulanate (10.7%), second-generation cephalosporins (3.8%), aminopenicillins without β-lactam inhibitors (2.4%) and other non-specified antibiotics (3.0%). For cardiovascular procedures, the non-compliant antibiotics were penicillinase-resistant penicillins (4.1%) and cefoxitin (1.0%) and for orthopaedic procedures the non-compliant antibiotics were mainly represented by cefalotin (2.1%), cefoxitin (1.1%) and penicillinase-resistant penicillins (0.8%). Table 4 shows the antibiotics most commonly prescribed for SAP (compliant and non-compliant) by surgical procedure.

In univariate analysis, antibiotic choice for SAP and total SAP duration were significantly associated with higher SSI incidence as well as the usual SSI risk factors, such as NNIS System risk index, pre-operative hospital stay, age and multiple procedures performed. Conversely, the timing of the first dose was not associated with SSI incidence (Table 2). In the multivariate analysis (Table 5), a too-short SAP duration remained the only inappropriate practice associated with higher SSI risk (OR=1.8, 95% CI: 1.14–2.81), after adjustment for surgery procedure group, NNIS System risk index and age. Table S1 [available as Supplementary data at *JAC* Online (http://jac.oxfordjournals.org/)] shows the output estimates of the final model.

Discussion

Based on a large survey including most important surgical procedures requiring SAP, we found that a too-short SAP duration, i.e. lack of intra-operative redosing despite the fact that it is

Table 4. Antibiotics most commonly prescribed for SAP, $N=7330$ surgery procedures

Antibiotic	Digestive ($N=1730$) *n* (%)	Gynaecology ($N=956$) *n* (%)	Orthopaedic ($N=3555$) *n* (%)	Cardiovascular ($N=1089$) *n* (%)
Cefazolin	144 (8.3)	**564 (59.0)**	**2123 (59.7)**	**277 (25.4)**
Cefamandole	11 (0.6)	23 (2.4)	**604 (17.0)**	**599 (55.0)**
Cefuroxime	7 (0.4)	13 (1.4)	**469 (13.2)**	**91 (8.4)**
Cefoxitin	**513 (29.7)**	98 (10.2)	40 (1.1)	11 (1.0)
Cefotetan	**91 (5.3)**	17 (1.8)	0 (0.0)	0 (0.0)
Amoxicillin/clavulanate	**578 (33.4)**	102 (10.7)	13 (0.4)	5 (0.5)
Vancomycin[a]	7 (0.4)	7 (0.7)	**139 (3.9)**	**38 (3.5)**
Other antibiotics	379 (21.9)	132 (13.8)	167 (4.7)	68 (6.2)

In bold, antibiotics recommended by the SFAR.[11]
[a]Vancomycin is an antibiotic recommended in cases of allergy to β-lactam antibiotics for orthopaedic and cardiovascular procedures.

recommended, was the most important SAP malpractice associated with an increased SSI risk. Other studies had shown the significance of intra-operative SAP redosing for preventing SSI risk.[27–29] A retrospective study, restricted to cardiac surgery, showed the benefit of intra-operative cefazolin redosing on SSI risk reduction.[27] Two randomized trials demonstrated the necessity for intra-operative cefazolin or cefoxitin redosing in various surgerical procedures that lasted >3 h.[28,29] These studies, however, were designed to prove an effect of SAP redosing on SSI risk. In contrast, we conducted a comprehensive study aiming to investigate which SAP practice parameters had a major role in SSI risk. SAP duration, more precisely a lack of intra-operative redosing, appeared to be the most important SAP malpractice parameter associated with an increased risk of SSI. Furthermore, our results were obtained using a multivariate regression analysis permitting adjustment for various risk factors, such as surgical procedures and patient conditions. Also, inter-hospital variability was measured using a two-level random intercept model allowing adjustment of the risk estimates for random variation among hospitals. van Kasteren *et al.*,[30] in a large survey on hip prosthesis with a study design similar to ours, did not find a significant relationship between SAP duration and SSI risk after comparable adjustment for confounders. However, this study did not assess compliance for each SAP parameter, in particular whether intra-operative redosing was recommended or not. To our knowledge, no other comparable published study has reported that poor compliance with this specific SAP recommendation was the most important malpractice associated with increased SSI rate.

Strikingly, lack of intra-operative redosing, despite the fact that it is recommended, was one of the most frequent malpractices, observed in almost 20%. This rate varied according to surgery; the highest non-compliance rate was for orthopaedic surgery procedures and the lowest for gynaecological procedures. According to recommendations, when the duration of a procedure is expected to exceed the time for which the active concentration of an antibiotic should be maintained, repeat intra-operative doses are indicated.[11,12] The recommended interval time for redosing (twice the half-life of the antibiotic) varies from 2 h to >4 h according to the antibiotic used. Although evidence-based guidelines exist to support the appropriateness of SAP practices, there is a substantial gap between these guidelines and their implementation in daily practice.[13–15] The awareness and knowledge of surgeons and anaesthesiologists could be improved using information and training based on standard recommendations as well as practice assessment study and morbidity–mortality reviews with root cause analysis of patient cases presenting with severe SSI.

Almost half of the SAP durations were too long, mainly in orthopaedic surgery where this proportion attained nearly 60%. This poor compliance could be partly explained by a discrepancy between French recommendations, which allow SAP duration to be extended up to 48 h for these particular procedures,[11] and the international standard used as the reference in our study, which is limited to 24 h.[12] Indeed, most studies reported that a 24 h regimen is often standard for orthopaedic or cardiovascular surgery.[7,14,31] Nonetheless, we did not find any significant relationship between too-long SAP duration and SSI risk. Indeed, as expected, too-long SAP duration fails to improve SSI risk. Besides, a too-long SAP duration carries a risk of multidrug-resistant bacteria selection. This result corroborates the issue that duration of SAP should be shortened to a maximum of 24 h after surgery.[17–19] More recently, studies comparing single-dose prophylaxis to multiple-dose prophylaxis did not show benefits of post-operative doses.[32–35]

Conversely to other studies,[20,36,37] we did not find that compliance with antibiotic choice or timing of first dose administration influenced SSI risk. This result could be explained partly by the fact that a small proportion of practices dismissed recommendations according to these two criteria. Regarding antibiotic choice for SAP, potential confounders that could influence SSI risk, such as NNIS System risk index or other peri-operative conditions, were taken into account in the final analysis. For example, the type of surgery was an important confounder factor. Indeed, antibiotic choice was significantly more often compliant in orthopaedic surgery (93.8%) than in non-orthopaedic surgery (73.4%), while the SSI risk in the latter was significantly higher (OR=7.6, 95% CI: 4.8–12.0). Thus, the crude OR of antibiotic choice (non-compliant versus compliant) was significantly associated with SSI risk (OR=2.1, 95% CI: 1.5–3.0; $P<0.0001$), whereas OR adjusted only for the type of surgery (non-orthopaedic versus orthopaedic) was not (adjusted OR 1.3, 95% CI: 0.95–1.8; $P=0.10$). In contrast, timing of the first dose was not associated with SSI risk, neither in univariate

Table 5. Risk factors for SSI in the multivariate logistic regression analysis, $N=6751$

	Random intercept model[a]			
	full model		final model	
Variable	OR (95% CI)	*P*	OR (95% CI)	*P*
Non-compliant antibiotic choice	1.2 (0.83–1.82)	0.30	—	—
Total duration of prophylaxis[b]				
compliant	ref.	ref.	ref.	ref.
too short	1.7 (1.11–2.73)	0.02	1.8 (1.14–2.81)	0.01
too long	1.2 (0.81–1.79)	0.35	1.2 (0.83–1.80)	0.32
Surgical procedure				
digestive	12.2 (7.07–21.13)	<0.001	13.5 (7.93–22.87)	<0.001
gynaecology	7.4 (3.64–15.22)	<0.001	8.3 (4.21–16.48)	<0.001
orthopaedic	ref.	ref.	ref.	ref.
cardiovascular	4.1 (2.03–8.17)		4.3 (2.14–8.50)	<0.001
NNIS System risk index[c]				
0	ref.	ref.	ref.	ref.
1	1.8 (1.24–2.66)	0.002	1.9 (1.30–2.78)	0.001
2	5.1 (2.92–8.77)	<0.001	5.4 (3.15–9.31)	<0.001
Age >40 years	3.1 (1.44–6.52)	0.004	3.2 (1.5–6.78)	0.003
Multiples procedures performed	1.2 (0.81–1.76)	0.36	—	—
Pre-operative hospital stay >48 h	1.4 (0.89–2.17)	0.15	—	—

	Model validation results	
	full model	final model
Log likelihood	−694.79	−696.69
−2LL (*P*)	<0.001	<0.001
Number of surgical procedures	6751	6751
Number of hospitals	132	132
Number of SSIs	171	171

[a]Output model obtained by retaining the significant variables ($P<0.05$).
[b]Non-compliance was categorized as: too-short duration, lack of intra-operative redosing despite the fact that it is recommended; and too-long duration, unnecessary re-injections or post-operative doses >24 h.
[c]Includes the following elements: ASA score, wound contamination class and duration of surgery.

nor in multivariate analysis. One could argue that a more detailed time stratification would have provided different results. However, when we stratified timing in intervals of $\leq$30 min, 31–60 min, 61–90 min and >90 min before incision and two classes for administration after incision ($\leq$30 or >30 min), no significant association was observed with SSI risk ($P=0.82$, Pearson χ^2 test). Whatever the methodological issues, we support the idea that timeliness of antibiotic administration is crucial. Several prior studies demonstrated that administering SAP >2 h before surgery resulted in lower tissue levels at the time of incision,[36] and administering SAP after the incision is closed fails to prevent contamination of the surgical wound.[20,37] However, in contrast with Classen *et al.*,[36] more recent evidence recommends a first administration of SAP within 60 min before incision.[12,14,20,37]

Our study has methodological strengths that should be emphasized. First, we analysed the correlation between the appropriateness of SAP practices and SSI risk using data from a large multicentre cohort of patients with all data collected prospectively by a standardized protocol that included post-discharge surveillance (up to 30 days after surgery). In addition, we used standard definitions for surveillance of SSI and standard evaluations of SAP practices. Furthermore, we analysed the effect of various parameters of SAP and several potential patient/procedure-specific risk factors on the risk of SSI by using a multilevel multivariate analysis that takes into account hospital effect.

Even though data were prospectively recorded from a large sample of participating surgery wards, our study had some limitations inherent to the design and the study population. First of all, there was a potential risk of selection bias, given that participation in the INCISO Surveillance Network is voluntary. However, since participation was anonymous, the motivation to deliver false or invalid data to the surveillance system is unlikely. In addition, we could analyse only the covariates that were reported within the network and some confounding variables that could have an impact on the SSI risk could have been missed (glucose control, hypothermia, blood loss, experience of the surgeon, pre-operative skin disinfection etc.). Also, because follow-up was limited to 30 days, some SSIs were probably missed. Although there was no modification in the SFAR recommendations[11] during the study period, SAP practices might have changed over time. Indeed, SSI rates decreased during the surveillance period,[21] probably owing to the feedback provided to the wards.

In conclusion, this study emphasizes the importance of intra-operative redosing according to antibiotic half-life and procedure duration, without undermining the role of timely administration described previously.[20,36,37] Information aimed at practitioners should be reinforced in order to improve compliance with SAP practices and eventually decrease SSI rates.

Acknowledgements

We thank the members of the INCISO Network Study Group [H. Blanchard (Paris), A. Chalfine (Paris), G. Cherbonnel (Evreux), Y. Costa (Lagny/Marne-la-Vallée), J. M. Germain (Rouen), B. Grandbastien (Lille), J. L. Jost (Paris), Z. Kadi (Amiens), M. Kitzis (Clichy), V. Merle (Rouen), L. Richard (Paris) and J. C. Séguier (Saint-Germain-en-Laye)] and the surgery wards for their participation in the INCISO Surveillance Network.

Funding

These data have been generated as part of the routine work of our INCISO Surveillance Network supported by the regional centre.

Transparency declarations

None to declare.

Supplementary data

Table S1 is available as Supplementary data at *JAC* Online (http://jac.oxfordjournals.org/).

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