

ORIGINAL ARTICLE

Risk Factors for Gram-Negative Bacterial Surgical Site Infection: Do Allergies to Antibiotics Increase Risk?

Jane V. Trinh, MD; Luke F. Chen, MBBS; Daniel J. Sexton, MD; Deverick J. Anderson, MD

OBJECTIVE. To determine the relationship between inadequate antimicrobial prophylaxis and development of gram-negative bacterial (GNB) surgical site infection (SSI).

DESIGN. Retrospective case-control study.

SETTING. A 369-bed acute care community hospital in Durham, North Carolina.

PATIENTS. Case patients were defined as patients who developed a GNB SSI after undergoing a surgical procedure during the period from January 1, 1998, through January 1, 2007. Control patients were uninfected patients who underwent surgery during the same study period and were matched to case patients by surgeon and type of procedure. Both patient groups were selected on the basis of prospectively collected data on patients who underwent surgery.

METHODS. Patient data were collected from patient medical records. Multivariable analysis was performed using logistic regression with backward selection, to identify variables independently associated with GNB SSI.

RESULTS. Case patients were similar to control patients with respect to demographics and comorbid conditions, but were older ($P = .04$), more obese ($P = .03$), and more likely to have diabetes mellitus ($P = .03$). Inappropriate timing of antimicrobial prophylaxis was the predominant reason that prophylaxis was deemed inadequate for both patient groups (59.1% of case patients vs 64.0% of control patients; $P = .56$). Case patients who had a history of allergic reactions to antimicrobial prophylaxis were significantly less likely to receive antimicrobial prophylaxis in a timely manner ($P = .03$). Variables independently associated with GNB SSI in multivariable analysis included urinary catheterization before surgery (odds ratio [OR], 3.74 [95% confidence interval {CI}, 1.11–12.62], diabetes mellitus (OR, 2.25 [95% CI, 1.02–4.94]), and an American Society of Anesthesiologists score greater than 2 (OR, 2.14 [95% CI, 1.13–4.06]).

CONCLUSIONS. A β -lactam allergy was not associated with increased risk for GNB SSI. Further studies, using patient data from larger hospital databases, are needed to examine the relationship between use of urinary catheter before surgery and risk of GNB SSI.

Infect Control Hosp Epidemiol 2009; 30:000-000

Surgical site infections (SSIs) are the second most common type of nosocomial infection, accounting for approximately one-quarter of all cases of nosocomial infection in the United States.^{1,2} Approximately 500,000 cases of SSI occur each year.^{3,4} SSIs can lead to adverse outcomes (which include prolonged hospitalization, hospital readmissions, and increased mortality) for patients who underwent a surgical procedure.^{1,5,6}

More than 50% of cases of SSI are caused by gram-positive organisms.⁷ As a result, most investigators have focused on gram-positive bacterial infections if performing studies on the epidemiology and outcomes of SSI.^{2,8} Even though gram-negative organisms account for approximately 20%–30% of cases of SSI reported to the National Nosocomial Infections Surveillance (NNIS) system for cardiac and total joint arthroplasty,⁹ there is a paucity of published data on risk factors for gram-negative bacterial (GNB) SSI.¹⁰

The Surgical Infection Prevention Project was established in 2002 by the Centers for Disease Control and Prevention and the Center for Medicaid and Medicare Services to improve the selection and timing of antimicrobial prophylaxis and thus decrease the morbidity and mortality associated with postoperative SSI.¹¹ The Surgical Infection Prevention Project guidelines for surgical antimicrobial prophylaxis consider β -lactam antibiotics with activity against gram-positive and gram-negative organisms to be the first line of therapy for patients undergoing a surgical procedure, and the guidelines recommend the use of agents such as clindamycin and vancomycin for patients with β -lactam allergies.^{11,12}

In daily practice, uncertainty about the exact nature of a β -lactam allergy often leads to the use of vancomycin for antimicrobial prophylaxis during surgery.¹³ However, vancomycin has no activity against gram-negative organisms.

From the Duke University Medical Center, Durham, North Carolina (all authors).

Received September 17, 2008; accepted November 26, 2008; electronically published March 23, 2009.

© 2009 by The Society for Healthcare Epidemiology of America. All rights reserved. 0899-823X/2009/3005-00XX\$15.00. DOI: 10.1086/596612

TABLE 1. Demographic and clinical characteristics of case patients with gram-negative bacterial surgical site infection and control patients at an acute care community hospital in Durham, North Carolina, 1998–2007

Characteristic	Case patients (<i>n</i> = 101)	Control patients (<i>n</i> = 101)	<i>P</i>
Demographic			
Age, mean $\pm$ SD, years	60.9 $\pm$ 16.2	56.0 $\pm$ 16.7	.04
Male sex	34 (33.6)	45 (44.6)	.15
White race	65 (64.4)	70 (69.3)	.56
Body mass index, mean $\pm$ SD	31.9 $\pm$ 9.6	29.1 $\pm$ 8.9	.03
Admission from home	96 (95)	95 (94)	.99
Clinical^a			
Diabetes mellitus	23 (22.8)	21 (20.8)	.86
Diabetes mellitus with end organ damage	12 (11.9)	2 (3.0)	.03
Congestive heart failure	13 (12.9)	5 (5.0)	.10
Myocardial infarction	20 (19.8)	12 (11.9)	.18
Chronic obstructive pulmonary disease	9 (8.9)	9 (8.9)	.99
Peptic ulcer disease	7 (6.9)	5 (5.0)	.77
Peripheral vascular disease	9 (8.9)	4 (4.0)	.25
End-stage renal disease	7 (6.9)	3 (3.0)	.33
Cerebral vascular accident	7 (6.9)	3 (3.0)	.33
Cancer	15 (14.9)	12 (11.9)	.68
Metastatic cancer	2 (2.0)	2 (2.0)	.99
Receipt of chronic immunosuppressant drugs	6 (5.9)	5 (5.0)	.77
Charlson score $\geq$ 1 at hospital admission	19 (18.8)	10 (9.9)	.11
McCabe-Jackson score of 1	8 (7.9)	9 (9.0)	.81

NOTE. Data are no. (%) of patients, unless otherwise indicated. SD, standard deviation.

^a Comorbid conditions and severity of illness.

Thus, patients who receive vancomycin may actually be at an increased risk for acquiring a GNB SSI.

The primary objective of our study was to determine whether having a β -lactam allergy was associated with the development of a GNB SSI. The secondary objectives were 2-fold: (1) to examine the relationship between inadequate antibiotic prophylaxis and the risk of GNB SSI and (2) to examine other risk factors associated with GNB SSI.

METHODS

We performed a retrospective case-control study of surgical patients admitted to a 369-bed acute care community hospital in Durham, North Carolina, during the period from January 1, 1998, to January 1, 2007. The study was approved by the institutional review board.

Identification of Patients

Case patients were defined as adult patients (ie, more than 18 years of age) diagnosed with a GNB SSI after undergoing a surgical procedure during the period from January 1, 1998, to January 1, 2007. Case patients were retrospectively identified by searching the Duke Infection Control Outreach Network surgical database that contained prospectively collected data on all surgeries performed at the study hospital.¹⁴ The data from this surgical database included patient demographic characteristics, date of surgery, length of procedure, and type

of procedure (by use of the NNIS code) for all surgical procedures. Data on the type of pathogen causing the SSI and the date the specimens were collected for culture were recorded in this surgical database.

SSIs were prospectively identified by trained infection control professionals using standard criteria from the Centers for Disease Control and Prevention.⁷ Patients were identified as having a SSI by a combination of the following: a review of microbiology culture reports, screening of patients for readmission to the hospital after surgery, and clinical rounds. In addition, hospitals used questionnaires to identify cases of SSI that occurred after hospital discharge. These questionnaires, which were sent quarterly to individual surgeons, contained a list of patients on whom that surgeon had recently performed surgery.¹⁴ Cases of GNB SSI included all cases of SSI in which at least 1 gram-negative organism had been isolated from a microbiological specimen (ie, a culture that yielded either a gram-negative organism, a mixture of gram-negative and gram-positive organisms, or a mixture of a gram-negative organism and some other type of organism). Cases of SSI with negative culture results and cases of SSI due to an unspecified mixture of organisms, to *Bacteroides* species, or to a gram-positive organism were excluded.

Control patients were matched to case patients at a 1 : 1 ratio on the basis of 2 factors: operating surgeon and surgical procedure. That is, each control patient underwent the same

TABLE 2. Perioperative data on case patients with gram-negative bacterial surgical site infection and control patients at an acute care community hospital in Durham, North Carolina, 1998–2007

Patient data	Case patients (<i>n</i> = 101)	Control patients (<i>n</i> = 101)	<i>P</i>
Documented antibiotic allergy	36 (35.6)	25 (24.7)	.13
ASA score >2	54 (56.8)	33 (33.3)	<.001
ICU admission before surgery	2 (2.0)	1 (1.0)	.62
Presence of central line before surgery	6 (6.1)	7 (6.3)	.99
Presence of an indwelling urinary catheter	12 (12.1)	5 (5.0)	.08
Median duration of surgery (IQR), minutes	160 (101–240)	117 (71–177)	.008
Temperature >38°C before surgery	6 (5.9)	0 (0)	.03
Skin preparation before surgery	97 (100)	96 (97)	.25
Hair removal before surgery	20 (21.1)	30 (30.6)	.14
Wound class >2	5 (4.9)	2 (2.0)	.25

NOTE. Data are no. (%) of patients, unless otherwise indicated. ASA, American Society of Anesthesiologists; ICU, intensive care unit; IQR, interquartile range.

surgical procedure by the same surgeon as the case patient to whom he or she was matched. Among patients who met these criteria, we selected uninfected patients who underwent an operation just prior to the matched case patient, to avoid any bias created by changes in surgical technique after a recent case of SSI (ie, the case patient).

All control patients were unique. Thus, if a control patient happened to be matched to more than 1 case patient with GNB SSI, then another uninfected patient was chosen as the control patient instead. Two control patients underwent procedures before January 1, 1998, because there were no uninfected patients available to match to 2 case patients during the period between January 1, 1998, and the date of each case patient's procedure.

Definition of Adequate Antimicrobial Prophylaxis

Two components of antimicrobial prophylaxis were examined for each set of case and control patients: the agent(s) used and the timing of administration. Antimicrobial prophylaxis was considered adequate if it met 2 criteria: (1) at least 1 of the antibiotics administered was recommended by published guidelines, and (2) the antibiotic was administered correctly (ie, within 1 hour before surgery for all agents except vancomycin and ciprofloxacin, which were allowed to be ad-

ministered 2 hours before surgery).^{11,12} Patients who underwent procedures for which no antimicrobial prophylaxis was indicated and in whom no prophylaxis was given were considered to have received adequate antimicrobial prophylaxis. If antimicrobial prophylaxis did not meet the above-mentioned criteria, it was defined as inadequate.

The administration of oral neomycin and erythromycin was considered adequate for colorectal procedures if the timing was consistent with published guidelines (ie, initiated no more than 18–24 hours before the operation, along with a mechanical bowel preparation).¹¹ Finally, for exploratory laparotomy procedures (surgical procedures with NNIS code XLAP, for exploratory abdominal surgery), antimicrobial prophylaxis was considered adequate if the antibiotics used were the same as those recommended for colorectal surgical procedures.

Definition of Allergy

All antimicrobial allergy data obtained from a patient's chart were recorded, including drug(s) used and reaction of patient. If a specific reaction to an antimicrobial agent was not provided in the chart, it was labeled as "unknown reaction." All patients with documented β -lactam allergies were considered to be β -lactam allergic, regardless of the reaction described.

TABLE 3. Data on preoperative antibiotic use for case patients with gram-negative bacterial surgical site infection and control patients at an acute care community hospital in Durham, North Carolina, 1998–2007

Data on antibiotic use	Case patients	Control patients	<i>P</i>
Preoperative antibiotics administered	98/101 (97.0)	100/101 (99.0)	.62
Adequate antimicrobial prophylaxis	51/98 (52.0)	57/100 (57.0)	.57
Appropriate antimicrobial agent	73/98 (74.5)	80/100 (80.0)	.49
Appropriate timing of administration	58/98 (59.1)	64/100 (64.0)	.56
Vancomycin administered	22/98 (22.4)	12/100 (12.0)	.09
Appropriate timing of vancomycin administration	13/22 (59.1)	6/12 (50.0)	.72

NOTE. Data are proportion (%) of patients.

TABLE 4. Preoperative data on antibiotic use for case patients with gram-negative bacterial surgical site infection and documented antibiotic allergies and control patients with documented antibiotic allergies at an acute care community hospital in Durham, North Carolina, 1998–2007

Type of allergy, data on antibiotic use	Case patients	Control patients	P
Any antibiotic allergy			
Adequate antimicrobial prophylaxis	17/35 (48.6)	17/25 (68.0)	.19
Appropriate antimicrobial agent	23/35 (65.7)	20/25 (80.0)	.26
Appropriate timing	18/35 (51.4)	20/25 (80.0)	.03
Any β -lactam allergy			
Adequate antimicrobial prophylaxis	12/23 (52.2)	9/14 (64.3)	.52
Appropriate antimicrobial agent	13/23 (56.5)	10/14 (71.4)	.49
Appropriate timing	11/23 (47.8)	12/14 (85.7)	.04
Vancomycin administered	12/23 (52.2)	5/14 (35.7)	.49
Appropriate timing of vancomycin administration	7/12 (58.3)	4/5 (80.0)	.60

NOTE. Data are proportion (%) of patients.

Data Collection

We conducted a retrospective chart review of case patients and control patients to collect data on patient demographics, hospital admissions, and clinical and microbiological characteristics and outcomes. McCabe-Jackson and Charlson scores were calculated for both case and control patients.^{15,16}

Data on mortality were obtained from hospital charts and the Social Security Death Index (available at: <http://ssdi.rootsweb.ancestry.com>). Data were collected on the following variables: admission source, admitting service, readmission diagnosis and date, American Society of Anesthesiologists (ASA) score, receipt of skin preparation and hair removal, type and duration of procedure, and wound class. The presence of an indwelling urinary catheter prior to surgery was recorded. Data on preoperative antimicrobial prophylaxis (ie, type and timing of prophylactic antibiotic therapy) were collected from electronic preoperative anesthesia records, to determine whether antimicrobial therapy was intended as treatment for a preexisting (ie, preoperative) infection or as treatment for a suspected infection. The resistance patterns of the isolates recovered from case patients with GNB SSI were evaluated by review of the paper and electronic medical charts. Data from 10% of the charts were reviewed by a second member of the study team, to confirm procedures during chart abstraction.

Statistical Analysis

Data were entered into a database (Access; Microsoft). Statistical analyses were performed using SAS, version 9.1 (SAS). Bivariable analyses for categorical variables were performed by use of the Fisher exact test or the χ^2 test. The Student *t* test was used for continuous variables. The Cochran-Armitage test for trend and the χ^2 test for trend were used to compare differences in the rates of SSI during the study period. A 2-tailed α of <.05 was considered to indicate a statistically significant difference for all tests.

Multivariable analysis was performed by use of logistic regression for dichotomous variables. Multivariable models

were constructed by use of a backward selection process. The reference model included all variables that had a *P* value of <.2 on bivariable analysis. If the β coefficients of model variables changed by 10% or more when a covariate was removed from the model, then the confounding covariate was retained in the final model.

RESULTS

During the 9-year study period, there were 52,804 surgical procedures in which 503 cases of SSI were identified. Of these 503 cases, 116 (23%) were GNB SSIs. Four patients were eliminated from our study, because matched control patients could not be found. Thus, the initial study cohort consisted of 112 case patients and 112 control patients.

In the post hoc analysis, 11 case patients were noted to have received antimicrobial treatment for a preexisting preoperative infection. As a result, surgical antimicrobial prophylaxis for these 11 case patients could not be assessed, and therefore these patients were excluded. The final study cohort consisted of 101 case patients and 101 control patients.

For the 101 case patients, the most common infecting gram-negative organisms were *Escherichia coli* (infecting 30 [29.7%] case patients), *Enterobacter* species (infecting 23 [22.8%] case patients), *Proteus* species (infecting 21 [20.8%] case patients), and *Pseudomonas* species (infecting 19 [18.0%] case patients). The median time from surgery to onset of a GNB SSI was 16 days (interquartile range [IQR], 10–25 days). Forty-four (43.6%) of the 101 case patients with GNB SSI had a mixture of a gram-negative organism and some other type of organism isolated from a microbiological specimen.

Although case patients and control patients were similar with respect to most demographic and clinical characteristics (Table 1), case patients were significantly older and more obese than control patients. The mean age ($\pm$ standard deviation [SD]) was 60.9 ± 16.2 years for case patients and 56.0 ± 16.7 years for control patients (*P* = .04). The mean body mass index ($\pm$ SD) was 31.9 ± 9.6 for case patients and 29.1 ± 8.9 for control patients (*P* = .03). More case patients

TABLE 5. Data on independent predictors of gram-negative surgical site infection at an acute care community hospital in Durham, North Carolina, 1998–2007

Risk factor	OR (95% CI)
Antibiotic allergy	1.39 (0.71–2.73)
Body mass index ≥ 30	1.88 (1.00–3.51)
ASA score >2	2.14 (1.13–4.06)
Diabetes with end organ damage	2.25 (1.02–4.94)
Presence of indwelling urinary catheter	3.74 (1.11–12.62)

NOTE. The reference model for our multivariable model included diabetes with end organ damage, congestive heart failure, myocardial infarction, Charlson and American Society of Anesthesiologists (ASA) scores, body mass index, receipt of vancomycin for antimicrobial prophylaxis, and presence of an indwelling urinary catheter at the time of surgery. CI, confidence interval; OR, odds ratio.

than control patients had diabetes mellitus with end organ damage (12 [11.9%] of 101 case patients vs 2 (3.0%) of 101 control patients; $P = .03$).

Orthopedic surgery and general surgery were the most common admitting services: of the 101 case patients, 41 (41.0%) underwent orthopedic surgery, and 36 (35.8%) underwent general surgery. There was no difference between case patients and control patients in the proportion of patients admitted to a particular service (data not shown).

Case patients had significantly higher ASA scores than did control patients (54 [56.8%] case patients vs 33 [33.3%] control patients; $P < .001$) (Table 2). Duration of surgery was longer for case patients (median time, 160 minutes [IQR, 101–240 minutes]) than for control patients (median time, 117 minutes [IQR, 71–177 minutes]; $P = .008$). There were no differences between case patients and control patients in the types of skin preparation or hair removal performed, wound class, rate of admission to the intensive care unit before surgery, or number of central line placements before surgery. Case patients used indwelling urinary catheters (12.1%) more frequently than did control patients (5.0%), but this difference only trended toward statistical significance ($P = .08$).

The number of case patients who received adequate antimicrobial prophylaxis was similar to the number of control patients who received adequate antimicrobial prophylaxis (Table 3). However, the numbers of case and control patients who received adequate antimicrobial prophylaxis before surgery were low (51 [52.0%] case patients and 57 [57.0%] control patients; $P = 0.57$). Inappropriate timing of antimicrobial prophylaxis was the predominant reason that prophylaxis was deemed inadequate in both groups of patients: 58 (59.1%) case patients and 64 (64.0%) control patients had inappropriately timed antimicrobial prophylaxis ($P = .56$). During the 9-year study period, however, the number of patients who received inadequate antimicrobial prophylaxis decreased ($P = .006$, for trend analysis); improvements were seen in both the selection of antibiotics ($P = .006$, for trend analysis) and the timing of antibiotic administration ($P =$

.004, for trend analysis). Rates of GNB SSI, however, only minimally improved from 0.28 to 0.24 cases of infection per 100 procedures during the study period, despite improvements in the administration of antimicrobial prophylaxis ($P = .99$, for trend analysis).

Case patients were more likely to receive vancomycin for antimicrobial prophylaxis than were control patients (22 [22.4%] case patients vs 12 [12.0%] control patients) (Table 3), but this did not reach statistical significance ($P = .09$). Both groups of patients encountered low hospital performance rates for appropriate timing of antimicrobial prophylaxis: 13 (59.1%) of 101 case patients and 6 (50.0%) of 101 control patients received vancomycin for antimicrobial prophylaxis at the appropriate time ($P = .72$).

Case patients were more likely to have an antibiotic allergy than were control patients (36 [35.6%] of 101 case patients vs 25 [24.7%] of 101 control patients; $P = .13$). Case patients who had a documented antimicrobial allergy were significantly less likely to receive antimicrobial prophylaxis in a timely manner than were control patients who had a documented antimicrobial allergy (18 [51.4%] of 35 case patients vs 20 [80.0%] of 25 control patients; $P = .03$) (Table 4). Case patients who had a documented allergy to β -lactam antibiotics were also less likely to receive antimicrobial prophylaxis in a timely manner than were control patients who had a documented allergy to β -lactam antibiotics (11 [47.8%] of 23 case patients vs 12 [85.7%] of 14 control patients; $P = .04$). Seven (58.3%) of 12 case patients who had an allergy to β -lactam agents received vancomycin at the appropriate time, whereas 4 (80.0%) of 5 control patients who had an allergy to β -lactam agents received vancomycin at the appropriate time ($P = .60$).

Case patients were more likely than control patients to be readmitted within 90 days after their surgical procedure (67 [66.3%] of 101 case patients vs 10 (9.9%) of 101 control patients; $P < .001$). There was no significant difference in mortality at 1 year between case patients and control patients (14 [13.8%] of 101 case patients died within 1 year after surgery vs 8 [7.9%] of 101 control patients died within 1 year after surgery; $P = .28$).

The variables used in our multivariable model included diabetes mellitus with end organ damage, congestive heart failure, myocardial infarction, the Charlson and ASA scores, the body mass index, receipt of vancomycin for antimicrobial prophylaxis, and the presence of an indwelling urinary catheter at the time of surgery. After the use of backward selection, the following variables were determined to be independently associated with the occurrence of a GNB SSI: the presence of an indwelling urinary catheter at the time of surgery (odds ratio [OR], 3.74 [95% confidence interval {CI}, 1.11–12.62]), diabetes mellitus with end organ damage (OR, 2.25 [95% CI, 1.02–4.94]), and an ASA score >2 (OR, 2.14 [95% CI, 1.13–4.06]) (Table 5). In the final model, we controlled for the confounding effects of body mass index and antibiotic allergy.

DISCUSSION

To our knowledge, our study is one of the largest studies on GNB SSI to evaluate specifically the relationship between inadequate antimicrobial prophylaxis and the development of GNB SSI. Although a β -lactam allergy was not associated with an increased risk of GNB SSI, case patients with GNB SSI who had any type of documented allergy were less likely to receive antimicrobial prophylaxis in a timely manner.

In general, the hospital performance rate for adequate antimicrobial prophylaxis was suboptimal for both groups of patients in our study. The primary reason for inadequate antimicrobial prophylaxis at the study hospital was inappropriate timing of antimicrobial prophylaxis. In fact, the hospital performance rates for timing of antimicrobial administration observed in this study population were consistent with the rates reported (by use of national surveillance data) for other hospitals prior to the implementation of Surgical Infection Prevention Project guidelines in 2002.^{9,17} Although inappropriate timing of antimicrobial prophylaxis for patients with antibiotic allergies was associated with the development of GNB SSI, our study was underpowered to analyze this association further. Overall, however, the hospital performance rates for appropriate antimicrobial prophylaxis improved during the study period.

We identified several risk factors for GNB SSI. Independent predictors of GNB SSI in our study included diabetes mellitus, an ASA score greater than 2, and the presence of an indwelling urinary catheter at the time of surgery. Although diabetes and an ASA score greater than 2 have been previously described as important risk factors for SSI,^{18–22} we demonstrate that the presence of a urinary catheter prior to surgery is also associated with an increased risk of GNB SSI.

The association between the presence of an indwelling urinary catheter prior to surgery and an increased risk of GNB SSI is unclear. Urinary tract infections have rarely been implicated as remote sources for SSI.²³ Other studies have demonstrated that any exposure to a urinary catheter is a risk factor for bloodstream infection or urinary tract infection,^{1,24} but few studies have examined the association between the presence of a urinary catheter and SSI, particularly in the absence of a urinary tract infection. A study of 3,180 patients who underwent orthopedic surgery demonstrated that long-term urinary catheterization (eg, the presence of an indwelling catheter for more than 21 days or after hospital discharge with catheter in situ) may play a role in the development of deep wound infections.²⁵ Colonizing organisms from the periurethral area are introduced at the time of catheter insertion.²⁶ Once colonization of the catheter occurs, the risk of bacteriuria increases daily.^{26,27} Thus, patients with indwelling catheters at the time of surgery may have higher rates of bacteriuria at the time of surgery. Because periurethral flora is typically with gram-negative bacteria, we hypothesize that this, in turn, may be a source for GNB SSI.

Our study had several limitations. Despite our initial co-

hort, which included 503 patients with SSI and involved 52,804 surgical procedures in 9 years, only 101 patients with GNB SSI were identified. The low number of case patients with GNB SSI limited our ability to examine risk factors for GNB SSI or to distinguish differences in the risk of GNB SSI between case patients undergoing clean (class I) surgical procedures and case patient undergoing nonclean (classes II and III) surgical procedures. Because the group of patients who received vancomycin as prophylaxis was a subgroup of our overall group, our study was likely underpowered to determine if receipt of vancomycin was a risk factor for GNB SSI. Similarly, we were unable to explore further the association between inappropriate timing of antimicrobial prophylaxis for patients with allergies, because of the small size of this subgroup ($n = 38$). Also, data related to antimicrobial therapy and clinical characteristics were obtained by manual chart review and, thus, may be subject to bias. In general, however, few variables had missing values. In addition, we used validated methods for data abstraction.^{21,28} In particular, data on antimicrobial therapy was abstracted from reliable electronic operating room records. Thus, we believe that it is less likely that our results were significantly statistically biased.

Despite the above-mentioned limitations, our study provides preliminary findings that warrant further investigation. More definitive assessments of specific risk factors for GNB SSI among patients who have undergone a clean procedure could be obtained by using larger hospital databases, especially with respect to vancomycin administration. Because cephalosporin use among patients with a penicillin allergy is often avoided, clarification of specific gram-negative coverage should be sought for those patients who receive vancomycin for antimicrobial prophylaxis; however, the timing of antimicrobial prophylaxis seems to be just as important as the selection of antibiotics. In addition, the association between the presence of an indwelling urinary catheter prior to surgery and a GNB SSI should be evaluated further; if our finding that the presence of a urinary catheter increases the risk of GNB SSI is confirmed in subsequent studies, targeted strategies can be developed for the prevention of GNB SSI. Finally, the role played by the timing of antimicrobial prophylaxis in the development of an SSI in patients with documented allergies should be further investigated.

ACKNOWLEDGMENTS

We thank Sarah Wilkins and Stephen Harward for data collection and the Durham Regional Hospital Infection Control Team for the maintenance of the infection control operative databases.

Potential conflicts of interest. D.J.A. is the recipient of the Pfizer Fellowship in Infectious Disease and has received research funding from Merck. All other authors report no conflicts of interest relevant to this article.

Address reprint requests to Jane V. Trinh, MD, Duke University Medical Center, 4020 North Roxboro Street, Box 3675, Durham, North Carolina 27704 (jane.trinh@duke.edu).

Presented in part: 48th Annual Interscience Conference on Antimicrobial

Agents and Chemotherapy/46th Annual Meeting of the Infectious Diseases Society of America; Washington, DC; October 25–28, 2008 (Abstract 1506).

REFERENCES

- Burke JP. Infection control—a problem for patient safety. *N Engl J Med* 2003; 348:651–656.
- National Nosocomial Infections Surveillance (NNIS) report, data summary from October 1986–April 1996, issued May 1996. A report from the National Nosocomial Infections Surveillance (NNIS) system. *Am J Infect Control* 1996; 24:380–388.
- Gaynes RP, Culver DH, Horan TC, Edwards JR, Richards C, Tolson JS. Surgical site infection (SSI) rates in the United States, 1992–1998: the National Nosocomial Infections Surveillance system basic SSI risk index. *Clin Infect Dis* 2001; 33(suppl 2):S69–S77.
- Edmiston CE Jr, Seabrook GR, Johnson CP, Paulson DS, Beausoleil CM. Comparative of a new and innovative 2% chlorhexidine gluconate-impregnated cloth with 4% chlorhexidine gluconate as topical antiseptic for preparation of the skin prior to surgery. *Am J Infect Control* 2007; 35: 89–96.
- Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. *Infect Control Hosp Epidemiol* 1999; 20:725–730.
- Perencevich EN, Sands KE, Cosgrove SE, Guadagnoli E, Meara E, Platt R. Health and economic impact of surgical site infections diagnosed after hospital discharge. *Emerg Infect Dis* 2003; 9:196–203.
- Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR; Hospital Infection Control Practices Advisory Committee. Guideline for prevention of surgical site infection, 1999. *Infect Control Hosp Epidemiol* 1999; 20:250–278.
- Engemann JJ, Carmeli Y, Cosgrove SE, et al. Adverse clinical and economic outcomes attributable to methicillin resistance among patients with *Staphylococcus aureus* surgical site infection. *Clin Infect Dis* 2003; 36: 592–598.
- Bratzler DW, Hunt DR. The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. *Clin Infect Dis* 2006; 43:322–330.
- Gaynes R, Edwards JR. Overview of nosocomial infections caused by gram-negative bacilli. *Clin Infect Dis* 2005; 41:848–854.
- Bratzler DW, Houck PM. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Clin Infect Dis* 2004; 38:1706–1715.
- Antimicrobial prophylaxis for surgery. *Treat Guidel Med Lett* 2006; 4:83–88.
- Osmon DR. Antimicrobial prophylaxis in adults. *Mayo Clin Proc* 2000; 75:98–109.
- Anderson DJ, Sexton DJ, Kanafani ZA, Auten G, Kaye KS. Severe surgical site infection in community hospitals: epidemiology, key procedures, and the changing prevalence of methicillin-resistant *Staphylococcus aureus*. *Infect Control Hosp Epidemiol* 2007; 28:1047–1053.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40:373–383.
- McCabe WR. Gram-negative bacteremia. *Adv Intern Med* 1974; 19:135–158.
- Bratzler DW, Houck PM, Richards C, et al. Use of antimicrobial prophylaxis for major surgery: baseline results from the National Surgical Infection Prevention Project. *Arch Surg* 2005; 140:174–182.
- Olsen MA, Mayfield J, Laurysen C, et al. Risk factors for surgical site infection in spinal surgery. *J Neurosurg* 2003; 98:149–155.
- Harrington G, Russo P, Spelman D, et al. Surgical-site infection rates and risk factor analysis in coronary artery bypass graft surgery. *Infect Control Hosp Epidemiol* 2004; 25:472–476.
- Wilson SJ, Sexton DJ. Elevated preoperative fasting serum glucose levels increase the risk of postoperative mediastinitis in patients undergoing open heart surgery. *Infect Control Hosp Epidemiol* 2003; 24:776–778.
- Kaye KS, Sloane R, Sexton DJ, Schmader KA. Risk factors for surgical site infections in older people. *J Am Geriatr Soc* 2006; 54:391–396.
- Simpson JM, Silveri CP, Balderston RA, Simeone FA, An HS. The results of operations on the lumbar spine in patients who have diabetes mellitus. *J Bone Joint Surg Am* 1993; 75:1823–1829.
- Edwards LD. The epidemiology of 2056 remote site infections and 1966 surgical wound infections occurring in 1865 patients: a four year study of 40,923 operations at Rush-Presbyterian-St. Luke's Hospital, Chicago. *Ann Surg* 1976; 184:758–766.
- Maki DG, Tambyah PA. Engineering out the risk for infection with urinary catheters. *Emerg Infect Dis* 2001; 7:342–347.
- Cumming D, Parker MJ. Urinary catheterisation and deep wound infection after hip fracture surgery. *Int Orthop* 2007; 31:483–485.
- Tambyah PA, Halvorson KT, Maki DG. A prospective study of pathogenesis of catheter-associated urinary tract infections. *Mayo Clin Proc* 1999; 74:131–136.
- Stark RP, Maki DG. Bacteriuria in the catheterized patient. What quantitative level of bacteriuria is relevant? *N Engl J Med* 1984; 311:560–564.
- Kaye KS, Schmit K, Pieper C, et al. The effect of increasing age on the risk of surgical site infection. *J Infect Dis* 2005; 191:1056–1062.