Single-dose Antibiotic Prophylaxis in Regional Anesthesia

A Retrospective Registry Analysis

Hagen Bomberg, M.D., Denise Krotten, M.S., Christine Kubulus, M.D., Stefan Wagenpfeil, Ph.D., Paul Kessler, M.D., Thorsten Steinfeldt, M.D., Thomas Standl, M.D., André Gottschalk, M.D., Jan Stork, M.D., Winfried Meissner, M.D., Juergen Birnbaum, M.D., Thea Koch, M.D., Daniel I. Sessler, M.D., Thomas Volk, M.D., Alexander Raddatz, M.D.

ABSTRACT

Background: Catheter-related infection is a serious complication of continuous regional anesthesia. The authors tested the hypothesis that single-dose antibiotic prophylaxis is associated with a lower incidence of catheter-related infections.

Methods: Our analysis was based on cases in the 25-center German Network for Regional Anesthesia database recorded between 2007 and 2014. Forty thousand three hundred sixty-two surgical patients who had continuous regional anesthesia were grouped into no antibiotic prophylaxis (n = 15,965) and single-dose antibiotic prophylaxis (n = 24,397). Catheter-related infections in each group were compared with chi-square test after 1:1 propensity-score matching. Odds ratios (ORs [95% CI]) were calculated with logistic regression and adjusted for imbalanced variables (standardized difference more than 0.1).

Results: Propensity matching successfully paired 11,307 patients with single-dose antibiotic prophylaxis (46% of 24,397 patients) and with 11,307 controls (71% of 15,965 patients). For peripheral catheters, the incidence without antibiotics (2.4%) was greater than with antibiotic prophylaxis (1.1%, $P < 0.001$; adjusted OR, 2.02; 95% CI, 1.49 to 2.75, $P < 0.001$). Infections of epidural catheters were also more common without antibiotics (5.2%) than with antibiotics (3.1%, $P < 0.001$; adjusted OR, 1.94; 95% CI, 1.55 to 2.43, $P < 0.001$).

Conclusions: Single-dose antibiotic prophylaxis was associated with fewer peripheral and epidural catheter infections. **(ANESTHESIOLOGY 2016; 125:505-15)**

REGIONAL anesthesia improves perioperative and postoperative analgesia[1,2] and may reduce morbidity and mortality.[3–5] However, patients with continuous regional anesthesia are at risk of catheter-related infections, which are painful and prolong hospitalization.[6–8] Depending on the catheter insertion site, the incidence of infection is reported to range from 0 to 7% for peripheral catheters[9–12] and from 0.8 to 4.2% for epidural catheters.[7,13,14]

It is clearly established that single-dose antibiotic prophylaxis reduces the incidence of surgical site infection in general surgery, obstetrics, gynecology, traumatology, and orthopedics.[15–17] In such cases, there is a strong consensus that the antibiotics should be given before skin incision.[17,18] On the other hand, antibiotic prophylaxis is not recommended for some types of clean surgery.

Whether antibiotic prophylaxis reduces the risk of catheter-related infections remains unclear, with conflicting results reported in small studies.[14,19] We therefore tested the primary hypothesis that single-dose antibiotic prophylaxis is associated with a reduced incidence of continuous

What We Already Know about This Topic

- Epidural and perineural catheter–related infections are rare, but whether antibiotic prophylaxis used for surgical indications reduces this rare incidence is not known

What This Article Tells Us That Is New

- In the German Network for Regional Anesthesia database, 11,307 patients receiving epidural or perineural catheters and single-shot antibiotics were propensity matched with the same number of individuals who did not receive antibiotics
- The adjusted odds ratio for infection, primarily defined as the presence of at least two of the symptoms redness, edema, or pressure/pain leading to catheter removal, was 2.02 (95% CI, 1.4 to 2.8) for peripheral catheters and 1.94 (95% CI, 1.6 to 2.4) for nonobstetrical epidural catheters

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Submitted for publication January 26, 2016. Accepted for publication May 24, 2016. From the Department of Anaesthesiology, Intensive Care Medicine and Pain Medicine, Saarland University, University Medical Centre, Homburg/Saar, Germany (H.B., D.K., C.K., T.V., A.R.); Institute for Medical Biometry, Epidemiology and Medical Informatics, Saarland University, University Medical Centre, Homburg/Saar, Germany (S.W.); Department of Anaesthesiology, Intensive Care and Pain Medicine, Orthopaedic University Hospital, Frankfurt, Germany (P.K.); Department of Anaesthesiology and Intensive Care Therapy, Philipps University Marburg, Marburg, Germany (T. Steinfeldt); Department of Anaesthesia, Intensive and Palliative Care Medicine, Academic Hospital Solingen, Solingen, Germany (T. Standl); Department of Anaesthesiology, Intensive Care and Pain Medicine, Friederikenstift, Hannover, Germany (A.G.); Centre for Anaesthesiology and Intensive Care Medicine, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany (J.S.); Department of Anaesthesiology and Intensive Care, Jena University Hospital, Jena, Thuringia, Germany (W.M.); Department of Anaesthesiology and Operative Intensive Care Medicine, Charité Campus Virchow Klinikum and Campus Mitte, Charité University Medicine Berlin, Berlin, Germany (J.B.); Department of Anesthesiology and Critical Care Medicine, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany (T.K.); and Department of Outcomes Research, Anesthesiology Institute, Cleveland Clinic, Cleveland, Ohio (D.I.S.).

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catheter-related infection in adults. We considered peripheral nerve and epidural catheters separately because the risk of infection and potential severity differs considerably. Similarly, we distinguished epidural catheters for obstetrics from epidural catheters inserted for other indications. Secondarily, we evaluated the relative effect of antibiotic administration before and after catheter insertion.

Materials and Methods

Ethical approval for this study (Ärztekammer Saarland number Ha50/11) was provided by the Ethical Committee of the Ärztekammer Saarland, Saarbrücken, Germany (Chairperson San.-Rat Prof. Dr. Hermann Schieffer) on March 22, 2011. Written consent was waived as the data were anonymous (regulatory proof of protection of data privacy, Saarland commissioner, March 12, 2014).

In 2007, the German Society for Anesthesiology and Intensive Care Medicine (Nürnberg, Germany) established a network for safety in regional anesthesia. The German Network for Regional Anesthesia database collects preoperative, intraoperative, and postoperative data from treating physicians at 25 German centers who complete a standard form.[20] Data are collected concurrently with patient care by pain nurses or treating physicians and include detailed information about the medical conditions of patients having regional anesthesia along with the procedure and postoperative course.

The registry included 101,822 cases acquired between September 2007 and August 2014. Data integrity was evaluated according to specific rules to delete erroneously entered data and to delete cases with missing information. The relation between age, height, weight, and gender were verified. The range for weight was defined from 38 to 250 kg for men and from 39 to 250 kg for women. The minimum height and weight was the third percentile of 14-yr-old girls (150 cm, 39 kg) and boys (150 cm, 38 kg). The body mass index (BMI) was calculated and defined from 16 to 70 kg/m^2. All participating centers were aware of the German guideline to prevent catheter-related infection.[21] These include hand cleaning and disinfection, use of surgical mask, sterile gloves and gown, cap covering hair, shaving the insertion site, skin disinfection, aseptic sheeting, aseptic drugs, and sterile bandaging. The definition of multiple skin puncture was more than one skin puncture during a particular block procedure.

Case Selection

We included patients aged 14 yr or older who had peripheral or epidural catheters inserted for surgical procedures. For patients with more than one catheter (n = 4,205, 10.4% of 40,362), we considered only the initial procedure. Patients were excluded from our analysis when they were already taking antibiotics, had catheters in place for more than 14 days, or had catheters that were not inserted for the index surgical procedure.

Definition of Infection

Among the prospectively recorded details was whether patients were treated with single-dose antibiotic prophylaxis and the time of antibiotic administration relative to catheter insertion. Signs of infections were reported by pain nurses or physicians during postoperative ward rounds and verified by the treating physicians. Infections at the catheter insertion site were prospectively defined as previously described.[22,23] Catheter-related infections were defined as the presence of at least two of the followings: redness, edema, or pressure/pain leading to the removal of the catheter. In considering whether to make an infection determination or remove a catheter, clinicians considered reactive protein, leukocytosis, discharge of pus at the puncture site, fever not otherwise explained, or abscess formation at the insertion site with need for surgical drainage. Infection status was evaluated at least daily during surgical ward rounds. Data collection ended the day that catheters were removed.

Single-dose Antibiotic Prophylaxis

Whether patients were treated with intravenous single-dose antibiotic prophylaxis was entirely at the discretion of the attending surgeon. Routine single-dose antibiotic prophylaxis was based on the surgical procedure and recommended by the guidelines of the German working group of Hygiene in Hospital and Practice (table 1).[16,24] In other words, the use of antibiotics was determined by the surgical procedure rather than the use of an analgesic catheter. Participating hospitals identified the antibiotic regimens they used.

Endpoints

Our primary outcomes were the associations between single-dose antibiotic prophylaxis and the incidence of peripheral or epidural catheter–related infection. The secondary endpoint was the effect of antibiotic timing on the incidence of catheter-related infection, specifically the risk of catheter-related infection when antibiotic prophylaxis was given before or after catheter insertion. Any time from admission to the operating suites until catheter insertion was considered to be administration "before" insertion. Antibiotic administration between catheter insertion and the surgical incision was considered to be administration "after" insertion.

Data Analysis

Our main analysis (for primary and secondary endpoints) was based on propensity-matched groups, adjusted for variables that remained unbalanced. Secondarily, we used multivariable regression to estimate the independent effects of antibiotic administration.

Population characteristics are reported as standardized differences (STDs; nonantibiotic prophylaxis minus single-dose antibiotic prophylaxis divided by the pooled SD). We used chi-square statistics to compare unadjusted frequencies between patients without and with antibiotic prophylaxis.

Table 1. Typical Antibiotic Prophylaxis by Surgical Specialty

	Antibiotics	Antibiotics in Case of Penicillin Allergy
General surgery	Cephalosporins group 2 with or without metronidazole combination acylaminopenicillin or β-lactamase inhibitor	Cefazolin, cefuroxime, or clindamycin
Obstetrics	Cephalosporins group 2 with or without metronidazole combination Acylaminopenicillin or β-lactamase inhibitor	Cefazolin, cefuroxime, or clindamycin with or without aminoglycoside
Gynecology	Cephalosporins group 2 with or without metronidazole combination acylaminopenicillin or β-lactamase inhibitor	Cefazolin, cefuroxime, or clindamycin with or without aminoglycoside
Traumatology/ orthopedics	Cephalosporins group 1+2 with or without metronidazole combination, acylaminopenicillin or beta- lactamase inhibitor	Cefazolin, cefuroxime, or clindamycin with or without aminoglycoside
Urology	Cephalosporins group 2 with or without metronidazole combination, fluoroquinolones, aminoglycosides, acylaminopenicillin or β-lactamase inhibitor	Cefazolin, cefuroxime, or clindamycin with or without aminoglycoside
Others	Cephalosporins group 1 or 2 with or without metronidazole combination, acylaminopenicillin or β-lactamase inhibitor	Cefazolin, cefuroxime, or clindamycin with or without aminoglycoside

We developed a propensity score for each patient based on the potential confounders listed in table 2. Patients given single-dose antibiotic prophylaxis were matched to the patient with the closest propensity score who was not given prophylaxis, keeping the maximum difference in propensity score less than 0.05. The matching algorithm was nearest neighbor matching without replacement. The number needed to treat (NNT), based on the matched analysis, was estimated to determine the number of patients who would have to be given single-dose antibiotic prophylaxis to avoid one catheter-related infection.

As a sensitivity analysis, multivariable logistic regression was used to calculate odds ratios (ORs) with 95% CIs.

The analysis was adjusted for confounders including sex, BMI, American Society of Anesthesiologists (ASA) physical status score, diabetes, surgical specialty, interscalene, femoral, sciatic nerve, other peripheral catheter sites, thoracic epidural, lumbar epidural, multiple skin punctures, prolonged catheter duration, year of surgery, and hospital center. Collinearity was tested by Pearson or Spearman correlation coefficients. Variables with a positive or negative correlation more than 0.3 and less than 0.3 were excluded, respectively. Goodness of fit was assessed by Hosmer–Lemeshow tests.

As a further sensitivity analysis, subgroups of matched patients were compared. The subgroups we considered were prolonged catheter use, multiple skin puncture, BMI more than or equal to 25 kg/m^2, ASA score more than or equal to 3, age more than or equal to 65 yr, and diabetes.

For our secondary endpoint, patients given single-dose antibiotic prophylaxis before catheter insertion were matched to the patient with the closest propensity score who given single-dose antibiotic prophylaxis after insertion, keeping the maximum difference in propensity score less than 0.05. Propensity scores for each patient were based on the same potential confounders as for the main analysis listed in table 2. As a sensitivity analysis, multivariable logistic regression was used as for the main analysis and adjusted for the same confounders.

Covariable balance after propensity score matching was assessed with STDs. STDs exceeding 0.1 were considered imbalanced and adjusted. Matched patients without and with antibiotic prophylaxis were compared based on infection using McNemar test or conditional logistic regression, as appropriate.

Propensity score matching used Python essentials as an extension of SPSS version 22 (IBM, Germany). All data analyses were performed using SPSS Statistics 22 (IBM). Continuous variables are expressed as means and SD. Categorical variables are presented as absolute and relative frequencies. We considered two-sided $P \leq 0.05$ to indicate statistical significance.

Results

The final study population consisted of 40,362 cases, all with continuous catheters and information about single-dose antibiotic prophylaxis (fig. 1). This cohort was subdivided into the following groups: no antibiotic prophylaxis (n = 15,965) and single-dose antibiotic prophylaxis (n = 24,397).

Characteristics of the patients are presented in table 2 (left columns). Patients not given antibiotic prophylaxis were younger, more likely to be female, and less likely to be diabetics. Patients not given antibiotic prophylaxis were also more likely to have lumbar epidural catheters and less likely to have had peripheral nerve blocks or thoracic epidural catheters. They were also less likely to require multiple skin puncture or prolonged catheter duration.

Propensity matching successfully paired 11,307 patients with single-dose antibiotic prophylaxis (46% of 24,397 patients) and with 11,307 controls (71% of 15,965 patients). As seen in table 2 (right columns), patients without and with antibiotic prophylaxis were much better balanced on covariables as a result of propensity matching. However, an imbalance remained for surgical specialty (STD, 0.13), other peripheral catheter sites (STD, 0.11), lumbar epidural catheters (STD, 0.15), year of surgery (STD, 0.18), and hospital center (STD, −0.46). To be conservative, we included all of these factors in a multiple model when comparing the two groups for catheter-related infection.

Matched patients given single-dose antibiotic prophylaxis had significantly fewer peripheral catheter-related infections

Table 2. Unmatched and Matched Population Characteristics

	Before Matching			After Matching		
	No Antibiotics (n = 15,965)	Antibiotics (n = 24,397)	STD*	No Antibiotics (n = 11,307)	Antibiotics (n = 11,307)	STD*
Male	5,428 (34.0)	11,126 (45.6)	−0.23	4,942 (43.7)	5,185 (45.9)	−0.04
Age (yr)	51.1 ± 19.8	59.3 ± 17.6	−0.43	57.5 ± 18.5	56.6 ± 19.3	0.05
Body mass index (kg/m²)	27.9 ± 5.8	27.9 ± 5.6	0.03	27.9 ± 5.8	27.8 ± 5.8	0.02
ASA score 1	2,713 (17.0)	3,318 (13.6)	0.09	1,583 (14.0)	1,854 (16.4)	−0.07
ASA score 2	8,162 (51.1)	13,722 (56.2)	−0.10	5,442 (48.1)	5,345 (47.3)	0.02
ASA score 3	4,998 (31.3)	7,140 (29.3)	0.04	4,194 (37.1)	3,990 (35.3)	0.04
ASA score 4	92 (0.6)	217 (0.9)	−0.04	88 (0.8)	118 (1.0)	−0.03
Diabetes	1,388 (8.7)	2,897 (11.9)	−0.11	1,237 (10.9)	1,574 (13.9)	−0.09
General surgery	992 (6.2)	4,208 (17.3)	−0.35	992 (8.8)	1,279 (11.3)	−0.09
Obstetrics	4,020 (25.1)	927 (3.8)	0.64	425 (3.8)	634 (5.6)	−0.09
Gynecology	402 (2.5)	705 (2.9)	−0.02	360 (3.2)	486 (4.3)	−0.06
Trauma and orthopedics	9,837 (61.6)	17,082 (70.0)	−0.18	8,847 (78.2)	8,243 (72.9)	0.13
Urology	357 (2.3)	1,254 (5.1)	−0.16	357 (3.1)	395 (3.5)	−0.02
Other surgical specialty†	357 (2.3)	221 (0.9)	0.11	326 (2.9)	270 (2.4)	0.03
Peripheral catheters						
Interscalene	1,349 (8.4)	3,461 (14.2)	−0.18	1,349 (11.9)	1,124 (9.9)	0.06
Femoral	1,757 (11.0)	4,209 (17.3)	−0.18	1,756 (15.5)	1,510 (13.3)	0.06
Sciatic nerve	1,736 (10.9)	1,498 (6.1)	0.17	1,504 (13.3)	1,409 (12.5)	0.03
Others‡	2,359 (14.8)	3,784 (15.5)	−0.02	2,352 (20.8)	1,868 (16.5)	0.11
Neuraxial catheters						
Thoracic epidural	1,722 (10.8)	5,724 (23.5)	−0.34	1,690 (15.0)	2,000 (17.7)	−0.07
Lumbar epidural	7,042 (44.1)	5,721 (23.4)	0.45	2,656 (23.5)	3,396 (30.1)	0.15
Multiple skin puncture	2,089 (13.1)	4,562 (18.7)	−0.15	1,522 (13.5)	1,864 (16.5)	−0.08
Prolonged catheter use (4–14 d)	6,736 (42.2)	11,857 (48.6)	−0.13	5,904 (52.2)	5,381 (47.6)	0.09

Propensity matching was based on sex, age, body mass index, American Society of Anesthesiologists (ASA) physical status score, diabetes, surgical specialty, catheter site, year of surgery, and hospital center. Continuous variables are expressed as means ± SDs and categorical variables as numbers (%).
*Standardized differences (STD) are the difference in means or proportions (no antibiotics minus antibiotic prophylaxis) divided by the pooled SD. †Other surgical specialty includes vascular surgery, internal medicine, pediatric surgery, cardiac surgery, neurology, and neurosurgery. ‡Other peripheral catheters include infraclavicular, axillary, supraclavicular, suprascapular, psoas, and saphenous nerves.

(1.1%) compared to those without prophylaxis (2.4%, *P* < 0.001, NNT, 76). After adjustment for imbalanced covariables, no use of single-dose antibiotic prophylaxis remained an independent risk factor for peripheral catheter-related infections (adjusted OR, 2.02; 95% CI, 1.49 to 2.75, *P* < 0.001). This was also true for any peripheral site, interscalene (no antibiotics: 4.1 *vs.* antibiotics: 2.0%, *P* = 0.003; NNT, 47, adjusted OR, 1.76; 95% CI, 1.04 to 2.98, *P* = 0.03), femoral (no antibiotics: 3.4 *vs.* antibiotics: 1.7%, *P* = 0.002; NNT, 60; adjusted OR, 1.74; 95% CI, 1.07 to 2.81, *P* = 0.02), sciatic (no antibiotics: 1.8 *vs.* antibiotics: 0.3%, *P* = 0.001; NNT, 77; adjusted OR, 3.00; 95% CI, 1.27 to 7.10, *P* = 0.01), and other peripheral sites (no antibiotics: 1.2 *vs.* antibiotics: 0.4%, *P* = 0.02; NNT, 137; adjusted OR, 4.04; 95% CI, 1.59 to 10.26; *P* = 0.003).

There were no epidural catheter–related infections in the matched obstetric population, thus precluding further analysis in these patients. Among the remaining matched epidural patients, those given single-dose antibiotic prophylaxis had significantly fewer catheter-related infections (3.1%) compared to those without prophylaxis (5.2%, *P* < 0.001; NNT, 49).

After adjustment for imbalanced covariables, no use of single-dose antibiotic prophylaxis remained an independent risk factor for epidural catheter-related infections (adjusted OR, 1.94; 95% CI, 1.55 to 2.43; *P* < 0.001; table 3). This was also true for thoracic epidural (no antibiotics: 6.2 *vs.* antibiotics: 3.9%, *P* = 0.001; NNT, 41; adjusted OR, 2.11; 95% CI, 1.51 to 2.94; *P* < 0.001) and lumbar epidural (no antibiotics: 4.3 *vs.* antibiotics: 2.6%, *P* = 0.001; NNT, 59; adjusted OR, 1.71; 95% CI, 1.25 to 2.34; *P* = 0.001).

In subgroups of peripheral catheters, no use of single-dose antibiotic prophylaxis significantly increased the risk of catheter-related infection after the adjustment for imbalanced covariables in patients with prolonged catheter use (crude OR, 2.05; 95% CI, 1.44 to 2.92, *P* < 0.001), BMI more than or equal to 25 kg/m² (crude OR, 1.98; 95% CI, 1.36 to 2.87, *P* < 0.001; fig. 2), and femoral or axillary catheter (no antibiotics: 3.4 *vs.* antibiotics: 1.7%, *P* < 0.001; NNT, 58; crude OR, 2.07; 95% CI, 1.33 to 3.24, *P* = 0.001; adjusted OR, 1.84; 95% CI, 1.13 to 2.95; *P* = 0.014). This was also true for patients with catheter use less than 4 days (no antibiotics: 1.6 *vs.* antibiotics: 0.7%, *P* = 0.001; NNT, 117; crude OR, 2.30; 95% CI, 1.40 to 3.79, *P* = 0.001; adjusted OR, 1.83; 95% CI, 1.13 to 2.95; *P* = 0.014).

In subgroups of epidural catheters, no use of single-dose antibiotic prophylaxis significantly increased the risk of

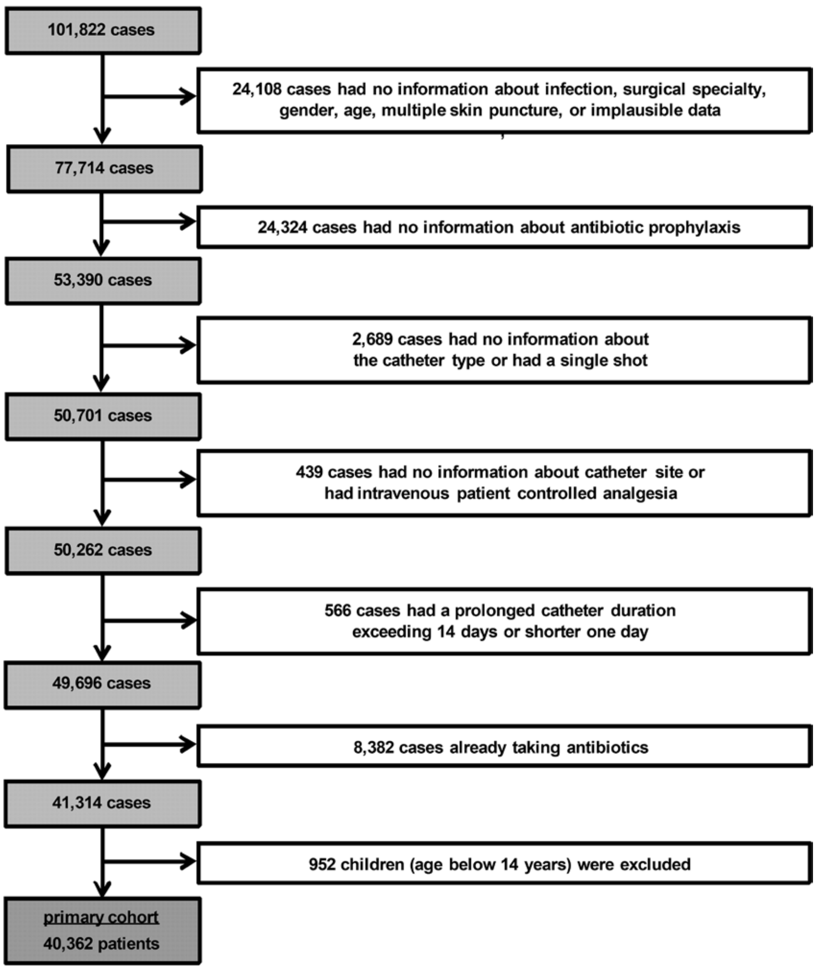

Fig. 1. Case selection.

catheter-related infection after the adjustment for imbalanced covariables in patients with prolonged catheter use (crude OR, 1.51; 95% CI, 1.18 to 1.94; $P = 0.001$), multiple skin puncture (crude OR, 1.77; 95% CI, 1.18 to 2.64, $P = 0.006$), BMI more than or equal to 25 kg/m^2 (crude OR, 2.14; 95% CI, 1.45 to 3.16; $P < 0.001$), ASA score more than or equal to 3 (crude OR, 1.75; 95% CI, 1.20 to 2.56, $P = 0.004$), and age more than or equal to 65 yr (crude OR, 2.09; 95% CI, 1.50 to 2.91; $P < 0.001$; fig. 3). This was also true for patients with catheter use less than 4 days (no antibiotics: 3.6 *vs.* antibiotics: 1.7%, $P = 0.001$; NNT, 53; crude OR, 2.16; 95% CI, 1.40 to 3.34, $P = 0.001$; adjusted OR, 2.38; 95% CI, 1.52 to 3.73; $P < 0.001$).

As a sensitivity analysis, we used multivariable regression to estimate treatment effects. Confounders that significantly influenced catheter-related infections were gender, BMI more than or equal to 25 kg/m^2, ASA physical status score more than or equal to 3, diabetes, surgical specialty, catheter site, multiple skin puncture, prolonged catheter duration (4 to 14 days), year of surgery, and hospital center. There was no collinearity between the confounders. After adjustment, single-dose antibiotic prophylaxis remained an independent preventive factor for catheter-related infections (table 3).

In 22,954 patients with single-dose antibiotic prophylaxis, timing of antibiotic administration relative to catheter insertion was available in 94% (n = 24,397). In 22,954 patients, 896 obstetrics were excluded resulting in the final study population for the timing of antibiotic administration of 22,058 patients. Characteristics of these patients are presented in table 4 (left columns). Propensity matching successfully paired 5,731 patients with single-dose antibiotic prophylaxis before (99% of 5,810 patients) and with 5,731 controls (35% of 16,248 patients). As seen in table 4 (right columns), patients with antibiotic prophylaxis before and after were much better balanced on covariables as a result of propensity matching. However, an imbalance remained for year of surgery (STD, −0.21) and hospital center (STD, −0.59). To be conservative, we included all of these factors in a multiple model when comparing the two groups for catheter-related infection. The incidence of catheter-related infections was similar in patients given antibiotics before and after catheter insertion (table 5). Multivariable

Table 3. Antibiotic Prophylaxis and Catheter-related Infections

	After Matching			
	No Antibiotics (n = 11,307)	Antibiotics (n=11,307)	Number Needed to Treat	*P* Value
Peripheral catheters (n/infections/%)	6,961/168/2.4	5,911/65/1.1	76	< 0.001
Crude OR (95% CI)	2.22 (1.67–2.97)		—	< 0.001
Adjusted OR (95% CI)	2.02 (1.49–2.75)		—	< 0.001
Non-OB epidural (n/infections/%)	3,921/202/5.2	4,762/148/3.1	49	< 0.001
Crude OR (95% CI)	1.69 (1.36–2.10)		—	< 0.001
Adjusted OR (95% CI)	1.94 (1.55–2.43)		—	< 0.001
Obstetrics epidural (n/infections/%)	425/0/0	634/0/0	—	—
	Sensitivity Analysis (before matching)			
	No Antibiotics (n = 15,965)	Antibiotics (n = 24,397)	Number Needed to Treat	*P* Value
Peripheral catheters (n/infections/%)	7,201/174/2.4	12,952/159/1.2	84	< 0.001
Crude OR (95% CI)	2.01 (1.62–2.50)		—	< 0.001
Adjusted OR (95% CI)	2.00 (1.45–2.78)		—	< 0.001
Non-OB epidural (n/infections/%)	4,744/229/5.2	10,518/317/3.1	55	< 0.001
Crude OR (95% CI)	1.63 (1.37–1.94)		—	< 0.001
Adjusted OR (95% CI)	1.94 (1.56–2.42)		—	< 0.001
Obstetrics epidural (n/infections/%)	4,020/8/0.2	927/0/0	503	0.17

Catheter-related infections are reported as group size/number of catheter-related infections/percentage of catheter-related infections. The number needed to treat was estimated to determine the number of patients who would have to be given single-dose antibiotic prophylaxis to avoid one catheter-related infection. Odds ratios (ORs) with 95% CI and adjusted for imbalanced variables (after matching) or potential confounders (before matching). The matched analysis was adjusted for surgical specialty, catheter site, year of surgery, and hospital center. The unmatched comparison was adjusted for gender, body mass index ≥ 25 kg/m², American Society of Anesthesiologists physical status score ≥ 3, diabetes, surgical specialty, catheter site, multiple skin puncture, prolonged catheter duration (4–14 days), year of surgery, and hospital center.

Non-OB = nonobstetrical.

regression similarly confirmed that there was no important effect of antibiotic timing on infection risk (table 5).

Discussion

ASA score, diabetes, surgery, multiple skin puncture, BMI, and prolonged catheter use have all been proposed as risk factors for catheter-related infection, with more or less supportive evidence.[7,8,11–13,19,22,23,25–27] In fact, each was shown to be independently associated with catheter-related infections in our analysis of 40,362 patients. But additionally, our analysis shows for the first time that single-dose antibiotic prophylaxis is strongly associated with reduced risk of catheter-related infection for both peripheral and epidural catheters.

The overall incidence of peripheral catheter-related infections was 1.7% in our study, which is consistent with previous reports.[9–12] In contrast, the 3.6% incidence of nonobstetrical epidural catheter–related infections was higher than previously reported.[13] Differences most likely result from varying definitions of infection and inflammation, patient population, prolonged catheter use, preventive hygiene measures, and probably many unknown factors. An advantage of our study is that the criteria for infection were clearly defined *a priori* and data collected prospectively.

The incidence of lumbar epidural catheter infections in obstetrics was low (0.16%). This may be explained by the typically short duration of catheter use in this population (1.4 ± 0.7 days). Antibiotic prophylaxis is thus unlikely to be a practical way to prevent catheter-related infections in this population.

It is well established that single-dose antibiotic prophylaxis decreases the risk of surgical site infections in general surgery, obstetrics, gynecology, traumatology, orthopedics, and urology.[15–17] Most surgeons use antibiotic prophylaxis covering skin microbes,[17] which also frequently colonize regional anesthesia catheters.[14,19,28] Moreover, single-dose antibiotic prophylaxis decreases the incidence of peritoneal dialysis catheter-related infection.[29] Our results strongly suggest that regional anesthesia catheter-related infections were decreased after single-dose antibiotic prophylaxis.

Nevertheless, widespread uncritical use of antibiotics as a cause of antibiotic resistance remains a major problem in the daily work in hospitals.[30,31] Therefore, the decision to use single-dose antibiotic prophylaxis only for catheter placement should consider risk and benefit, given the NNT of 49 for epidural catheters and 76 for peripheral nerve catheters.

The risk of catheter-related infections was reduced by single-dose antibiotic prophylaxis in all subgroups, including patients with prolonged catheter use (4 to 14 days) and those with a BMI more than or equal to 25 kg/m². Both

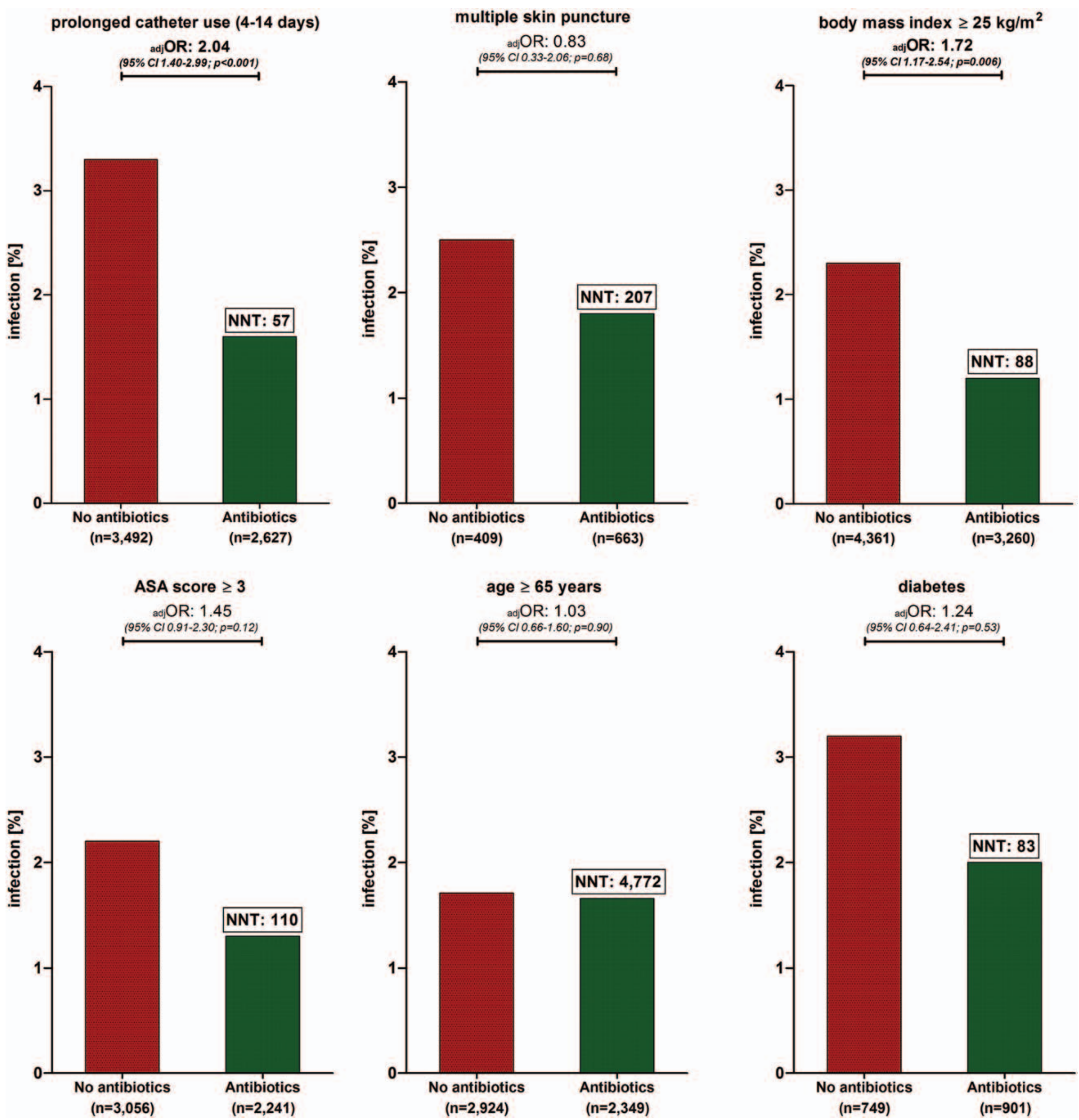

Fig. 2. Subgroup analysis for peripheral catheter–related infections. Subgroup analysis after 1:1 propensity score matching for peripheral catheters. The number needed to treat (NNT) is the estimated number of patients who would have to be given single-dose antibiotic prophylaxis to avoid one catheter-related infection. Odds ratios (ORs) and 95% confidence intervals (CIs) were adjusted for surgical specialty, catheter site, year of surgery, and hospital center. ASA score = American Society of Anesthesiologists physical status score.

subgroups have a known increased risk for catheter-related infection compared to the general population, suggesting that single-dose antibiotic prophylaxis might be especially useful in these populations.[12,22]

For epidural catheters, patients with multiple skin puncture and prolonged catheter use (4 to 14 days) have shown a significantly reduced risk of catheter-related infection and a NNT less than 100. Multiple skin puncture and prolonged catheter use are known risk factors for catheter-related infection, and single-dose antibiotic prophylaxis could be useful.[22]

It is common that single-dose antibiotic prophylaxis is administered before surgery but not before catheter placement. Previous studies found that single-dose antibiotic prophylaxis 20 to 30 min before surgery best reduced the risk of surgical site infections.[17,32] However, administration of

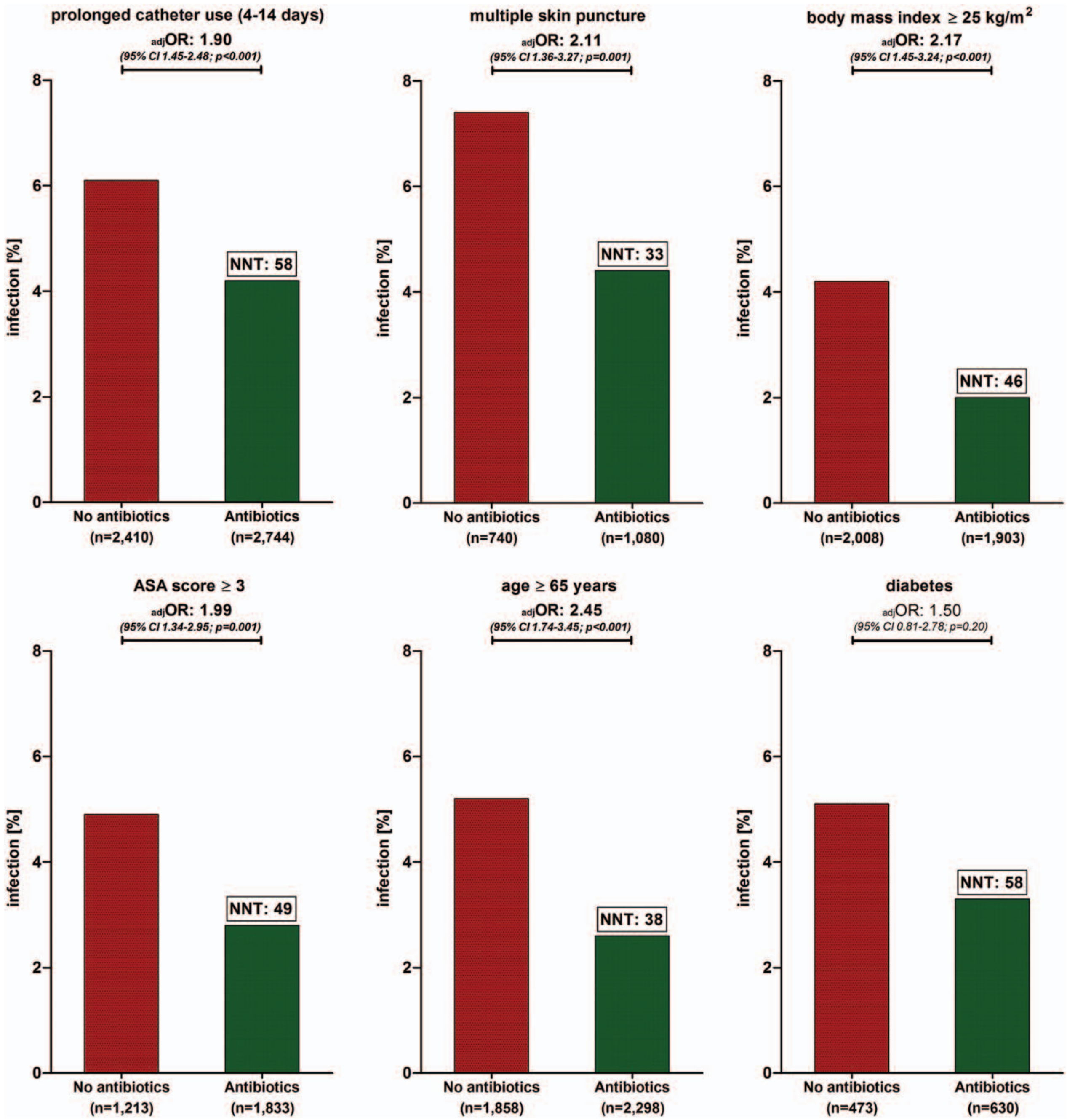

Fig. 3. Subgroup analysis for nonobstetrical epidural catheter–related infections. Subgroup analysis after 1:1 propensity score matching for epidural catheters. The number needed to treat (NNT) is the estimated number of patients who would have to be given single-dose antibiotic prophylaxis to avoid one catheter-related infection. Odds ratios (ORs) and 95% confidence intervals (CIs) were adjusted for surgical specialty, catheter site, year of surgery, and hospital center. ASA score = American Society of Anesthesiologists physical status score.

single-dose antibiotic prophylaxis immediately before or during surgery also reduces the risk of surgical site infection.[17,18]

We found no difference in infection rates when the antibiotic prophylaxis was given before or after catheter insertion. The elapsed time between catheter insertion and single-dose antibiotic prophylaxis is usually short because the surgery begins immediately thereafter, and antibiotics are virtually always given before surgical incision. Our results suggest that timing of prophylactic antibiotic administration is noncritical.

Our analysis was restricted to the risk of catheter-related infection for peripheral and epidural catheters. We do not have sufficient information on the method of treatment, longer term recovery, severity of infection, duration of hospitalization, or mortality. Consequently, we cannot determine whether the observed infections were linked to more serious

Table 4. Timing of Antibiotic Prophylaxis, Unmatched, and Matched Population Characteristics

	Before Matching			After Matching		
	Antibiotics Before Insertion (n = 5,810)	Antibiotics After Insertion (n = 16,248)	STD*	Antibiotics Before Insertion (n = 5,731)	Antibiotics After Insertion (n = 5,731)	STD*
Male	3,062 (52.7)	7,392 (45.5)	0.15	2,996 (52.3)	2,941 (51.3)	0.02
Age (yr)	60.5 ± 15.8	60.3 ± 17.5	0.01	60.5 ± 15.9	59.9 ± 16.5	0.04
Body mass index (kg/m^2)	28.1 ± 5.7	27.8 ± 5.6	0.05	27.6 ± 5.6	27.5 ± 5.2	0.02
ASA score 1	649 (11.2)	2,355 (14.5)	−0.10	647 (11.3)	642 (11.2)	0.00
ASA score 2	4,104 (70.6)	7,983 (49.1)	0.45	4,029 (70.3)	4,037 (70.4)	−0.00
ASA score 3	1,033 (17.8)	5,724 (35.2)	−0.40	1,031 (18.0)	1,032 (18.0)	−0.00
ASA score 4	24 (0.4)	186 (1.2)	−0.08	24 (0.4)	20 (0.4)	0.01
Diabetes	674 (11.6)	2,043 (12.6)	−0.03	667 (11.6)	647 (11.3)	0.01
General surgery	1,314 (22.6)	2,527 (15.6)	0.18	1,309 (22.9)	1,371 (23.9)	−0.03
Gynecology	103 (1.8)	521 (3.2)	−0.09	103 (1.8)	99 (1.7)	0.01
Trauma and orthopedics	3,643 (62.7)	12,591 (77.5)	−0.33	3,641 (63.5)	3,693 (64.5)	−0.02
Urology	637 (11.0)	525 (3.2)	0.31	579 (10.1)	494 (8.6)	0.05
Other surgical specialty†	113 (1.9)	84 (0.5)	0.13	99 (1.7)	74 (1.3)	0.04
Peripheral catheters						
Interscalene	1,028 (17.7)	2,275 (14.0)	0.10	1,027 (17.9)	1,136 (19.8)	−0.05
Femoral	1,696 (29.2)	2,259 (13.9)	0.38	1,690 (29.5)	1,637 (28.6)	0.02
Sciatic nerve	183 (3.1)	1,199 (7.4)	−0.19	182 (3.2)	188 (3.3)	−0.01
Others‡	475 (8.2)	3,090 (19.0)	−0.32	465 (8.1)	437 (7.6)	0.02
Neuraxial catheters						
Thoracic epidural	1,915 (33.0)	3,247 (20.0)	0.30	1,855 (32.4)	1,840 (32.1)	0.01
Lumbar epidural	513 (8.8)	4,178 (25.7)	−0.46	512 (8.9)	493 (8.6)	0.01
Multiple skin puncture	1,423 (24.5)	2,682 (16.5)	0.20	1,372 (23.9)	1,324 (23.1)	0.02
Prolonged catheter use (4–14 d)	3,077 (53.0)	7,888 (48.6)	0.09	3,040 (53.1)	3,064 (53.5)	−0.01

Propensity matching was based on sex, age, body mass index, American Society of Anesthesiologists (ASA) physical status score, diabetes, surgical specialty, catheter site, year of surgery, and hospital center. Continuous variables are expressed as means ± SDs and categorical variables as numbers (%).
*Standardized differences (STDs) are the difference in means or proportions (antibiotics before minus antibiotic after insertion) divided by the pooled SD. †Other surgical specialty includes vascular surgery, internal medicine, pediatric surgery, cardiac surgery, neurology, and neurosurgery. ‡Other peripheral catheters include infraclavicular, axillary, supraclavicular, suprascapular, psoas, and saphenous nerves.

outcomes. Moreover, patient comorbidities with potential influence for catheter-related infection are missing in our analysis, *i.e.*, severity of diabetes, stage of cancer, grade of renal failure, and amount of steroid use, or other immunosuppressive medication.

The basis of our documentation was clinical routine, which was then electronically transferred into the registry. The registry design was pragmatic, and the level of documentation thus varies somewhat from center to center. A university hospital has described this "gap" of documentation as 75%, and efforts are in progress to improve routine documentation.[33,34] Many cases were thus excluded because of missing information about infection and whether antibiotics were given. The high number of excluded patients increases the risk of bias in our analysis. And as in any nonrandomized analysis, residual confounding may introduce error, which will not be eliminated by our propensity-matched sensitivity analysis.

During the 7-yr observation period, there were presumably improvements in knowledge, skills, techniques, and disinfectant methods. However, our results were adjusted for the year of surgery. There was heterogeneity in the incidence of infection among the hospitals in our analysis and this was added as confounder in a multiple model. Because our population was large, it is possible to identify statistically significant associations that are not clinically important. However, the magnitude of the associations we observed are clearly clinically meaningful. Registries critically depend on the quality of data entry and handling; the validity of registry analyses thus always depends on the quality of the underlying data. Although our analysis was retrospective, infection data in our registry were specifically collected concurrent with patient care using *a priori* definition.

In summary, not using single-dose antibiotic prophylaxis was associated with an increased incidence of catheter-related infections in regional anesthesia, compared to patients with antibiotic prophylaxis. The risk of infection was significantly increased for peripheral catheters (adjusted OR, 2.02; NNT, 76) as well as for nonobstetrical epidural catheters (adjusted OR, 1.94; NNT, 49) and was largely consistent across various subgroups including those with prolonged catheter use, high BMI, and multiple skin punctures. In contrast, it made no apparent difference whether antibiotics were given before or after catheter insertion.

Table 5. Timing of Antibiotic Prophylaxis and Catheter-related Infections

	After Matching		
	Antibiotics Before Insertion (n = 5,731)	Antibiotics After Insertion (n = 5,731)	*P* Value
Peripheral catheters (n/infections/%)	3,364/43/1.3	3,398/55/1.6	0.24
Crude OR (95% CI)	0.79 (0.53–1.18)		0.24
Adjusted OR (95% CI)	0.91 (0.58–1.41)		0.66
Non-OB epidural (n/infections/%)	2,367/83/3.5	2,333/86/3.7	0.74
Crude OR (95% CI)	0.95 (0.70–1.29)		0.74
Adjusted OR (95% CI)	0.97 (0.70–1.34)		0.85
	Sensitivity Analysis (before matching)		
	Antibiotics Before Insertion (n = 5,810)	Antibiotics After Insertion (n = 16,248)	*P* Value
Peripheral catheters (n/infections/%)	3,382/43/1.3	8,823/102/1.2	0.60
Crude OR (95% CI)	1.10 (0.77-1.58)		0.60
Adjusted OR (95% CI)	0.76 (0.51–1.15)		0.19
Non-OB epidural (n/infections/%)	2,428/83/3.4	7,425/188/2.5	0.02
Crude OR (95% CI)	1.36 (1.05–1.77)		0.02
Adjusted OR (95% CI)	1.01 (0.75–1.35)		0.97

Catheter-related infections are reported as group size/number of catheter-related infections/percentage of catheter-related infections. Odds ratios (ORs) with 95% confidence intervals (CIs) and adjusted for imbalanced variables (after matching) or potential confounders (before matching). The matched analysis was adjusted for year of surgery and hospital center. The unmatched comparison was adjusted for gender, body mass index ≥ 25 kg/m^2, American Society of Anesthesiologists physical status score ≥ 3, diabetes, surgical specialty, catheter site, multiple skin puncture, prolonged catheter duration (4–14 d), year of surgery, and hospital center.

Non-OB = nonobstetrical.

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Correspondence

Address correspondence to Prof. Volk: Department of Anaesthesiology, Intensive Care Medicine and Pain Medicine, Saarland University Hospital, Kirrbergerstrasse 1, 66421 Homburg/Saar, Germany. thomas.volk@uks.eu. This article may be accessed for personal use at no charge through the Journal Web site, www.anesthesiology.org.

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