

# Prolonged Catheter Use and Infection in Regional Anesthesia

## A Retrospective Registry Analysis

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### ABSTRACT

**Background:** Prolonged catheter use is controversial because of the risk of catheter-related infection, but the extent to which the risk increases over time remains unknown. We thus assessed the time-dependence of catheter-related infection risk up to 15 days.

**Methods:** Our analysis was based on the German Network for Regional Anesthesia, which includes 25 centers. We considered 44,555 patients who had surgery between 2007 and 2014 and had continuous regional anesthesia as well as complete covariable details. Cox regression analysis was performed and adjusted for confounding covariables to examine the relationship between catheter duration and probability of infection-free catheter use.

**Results:** After adjustment for confounding factors, the probability of infection-free catheter use decreases with each day of peripheral and epidural catheter use. In peripheral catheters, it was 99% at day 4 of catheter duration, 96% at day 7, and 73% at day 15. In epidural catheters, it was 99% at day 4 of catheter duration, 95% at day 7, and 73% at day 15. Only 31 patients (0.07%) had severe infections that prompted surgical intervention. Among these were five catheters that initially had only mild or moderate signs of infection and were left *in situ*; all progressed to severe infections.

**Conclusions:** Infection risk in catheter use increases over time, especially after four days. Infected catheters should be removed as soon as practical.

**Visual Abstract:** An online visual overview is available for this article at <http://links.lww.com/ALN/B683>. (ANESTHESIOLOGY 2018; 128:764-73)

CONTINUOUS regional anesthesia improves perioperative analgesia<sup>1,2</sup> and may reduce morbidity and mortality.<sup>3-5</sup> However, long-term catheter use increases the risk of catheter-related infections,<sup>6-9</sup> which are painful, increase morbidity, and prolong hospitalization.<sup>10-12</sup> Depending on the catheter insertion site, the incidence of infection reportedly ranges from 0 to 7% for peripheral catheters.<sup>9,13-15</sup> For epidural catheters, reported risk ranges from 0.8 to 4.9%.<sup>6,11,16,17</sup>

The extent to which the risk of catheter-related infection increases with catheter duration remains unclear—in part because previous influential studies do not clearly define prolonged catheter use,<sup>6-9</sup> and perhaps by the fact that the duration of peripheral nerve and epidural catheter use differs considerably by country: in the United States, typical maximum catheter duration is reported to be 1 to 4 days<sup>18,19</sup>; in Switzerland, 1.5 to 5 days<sup>14,20</sup>; in Australia, 1 to 13 days<sup>6</sup>; and in Germany, 1 to 36 days.<sup>8,9,16,17</sup> Which approach is preferable remains unknown. We therefore evaluated the extent to which peripheral nerve and epidural catheter-related infections increase over time in adults using a prospective

#### What We Already Know about This Topic

- Prolonged use of indwelling peripheral nerve blockade or epidural catheters may be associated with infection
- Multicenter, pragmatic data guiding duration of catheter use are not available

#### What This Manuscript Tells Us That Is New

- Ninety-nine percent of peripheral catheters and ninety-nine percent of epidural catheters were infection-free after four days
- Infected catheters should be removed as soon as is practical

voluntary national multicenter registry in Germany. We hypothesized that each additional day of catheter use is associated with an increased risk of catheter-related infection.

#### Materials and Methods

Approval for this study was provided by the Ethics Committee of the Saarland Medical Chamber, Saarbrücken, Germany (Chairperson, Sanitätsrat Prof. Dr. Hermann

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Schieffer) on March 22, 2011, with the identification No. Ha50/11. 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 and the Professional Association of German Anesthesiologists (Nuremberg, 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 completed a standard form (appendix 1).<sup>21</sup> Data from patients having regional anesthesia included detailed information about their medical conditions along with the procedure and postoperative course. These data were collected by pain nurses or treating physicians concurrently with patient care. The data were entered contemporaneous with standard documentation and were collected electronically or on paper.

This registry includes 114,543 cases acquired between September 2007 and December 2014. The study protocol is reported in appendix 2. Data integrity was evaluated according to specific rules to delete erroneously entered data as well as cases with missing information (proof of plausibility, appendix 2). The body mass index (BMI) was calculated as weight in kg/(size in m)<sup>2</sup> and defined from 17 to 70 kg/m<sup>2</sup>. All participating centers were aware of the German guidelines to reduce catheter-related infection.<sup>22</sup> 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.

Submitted for publication May 2, 2017. Accepted for publication December 27, 2017. From the Department of Anesthesiology, Intensive Care Medicine and Pain Medicine (H.B., I.B., T.V., A.R.), and the Institute for Medical Biometry, Epidemiology and Medical Informatics (S.W.), Saarland University, University Medical Center, Homburg/Saar, Germany; the Department of Anesthesiology, Intensive Care and Pain Medicine, Orthopedic University Hospital, Frankfurt, Germany (P.K.); the Department of Anesthesiology and Intensive Care Therapy, Philipps University Marburg, Germany (H.W.); the Department of Anesthesia, Intensive and Palliative Care Medicine, Academic Hospital Solingen, Germany (T.S.); the Department of Anesthesiology, Intensive Care and Pain Medicine, Friederikenstift Hannover, Germany (A.G.); the Department of Anesthesiology and Intensive Care Medicine, Hospital Calw-Nagold, Germany (J.D.); the Department of Anesthesiology, St. Marien-Hospital, Siegen, Germany (W.H.); the Department of Anesthesiology and Operative Intensive Care Medicine, Charité Campus Virchow Klinikum and Campus Mitte, Charité University Medicine Berlin, Germany (J.B., C.S.); the Department of Anesthesiology, Intensive Care and Pain Therapy, University and Rehabilitation Clinics, Ulm, Germany (B.K., J.W.); the Department of Anesthesiology, Intensive Care and Pain Therapy, HELIOS Hospital Erfurt, Germany (S.L.-B.); the Department of Anesthesiology and Intensive Care, Jena University Hospital, Germany (W.M.); the Department of Anesthesiology, Intensive Care Medicine, University Hospital Carl Gustav Carus, Technische Universität Dresden, Germany (O.V., T.K.); and the Department of Outcomes Research, Anesthesiology Institute, Cleveland Clinic, Cleveland, Ohio (D.I.S.).

### Case Selection

We included patients 0 to 100 yr old who had peripheral or epidural catheters inserted for surgical procedures, information about catheter *in situ* time, and information about catheter-related infection. Patients were excluded from our analysis when catheters were in place for more than 15 days—a rare event. Catheters used for obstetric analgesia were also excluded because they are rarely used for more than 48 h (fig. 1).<sup>23</sup>

### Definition of Infection

Among the prospectively recorded details was the catheter duration. Signs of infections were reported by pain nurses or physicians during postoperative ward rounds. Infections at the catheter insertion site were prospectively defined as previously described<sup>24,25</sup>: (1) mild infections were defined by at least two of three infection signs (redness, swelling, or local pain); (2) moderate infections were defined as mild in addition to at least one of the following findings: increased C-reactive protein, leucocytosis, fever, or pus at the punctured site; and (3) severe infections were defined by the need for a surgical incision or revision. Infection status was evaluated at least daily during surgical ward rounds. Data collection ended when catheters were removed.

### Endpoints

The primary endpoint was a composite of the presence of a mild, moderate, or severe catheter-related infection up to 15 days. The secondary endpoint was progression of low-grade (mild/moderate) infection of catheters left *in situ* to higher-grade (moderate/severe) infections.

### Data Analysis

Each patient with prolonged catheter use was included only with the first observed infection. Population characteristics are reported as absolute standardized differences (absolute value of means [infection-free catheter use minus catheter-related infection] divided by the pooled SD).

A Kaplan–Meier survival curve was plotted to examine the relationship between catheter duration and probability of infection-free catheter use. Cox regression analysis was performed, and an adjusted survival curve was plotted. Cox regression survival curves were estimated using the default setting of SPSS Statistics 19 (IBM, USA): a patient with the mean of all covariates. This analysis was used in the final study population: patients with a complete set of covariates, which are specified in tables 1 and 2. Potential confounders were sex, age, BMI, American Society of Anesthesiologists physical status, diabetes, multiple skin puncture, surgical specialty, catheter site, year of surgery, and hospital. Age and BMI were included as continuous variables; all other covariates were included as categorical variables. Variables with a positive or negative correlation greater than 0.3 and less than or equal to −0.3 were evaluated for interactions. The assumption of proportional hazard was checked for all included variables. An omnibus test was performed to calculate *P* value

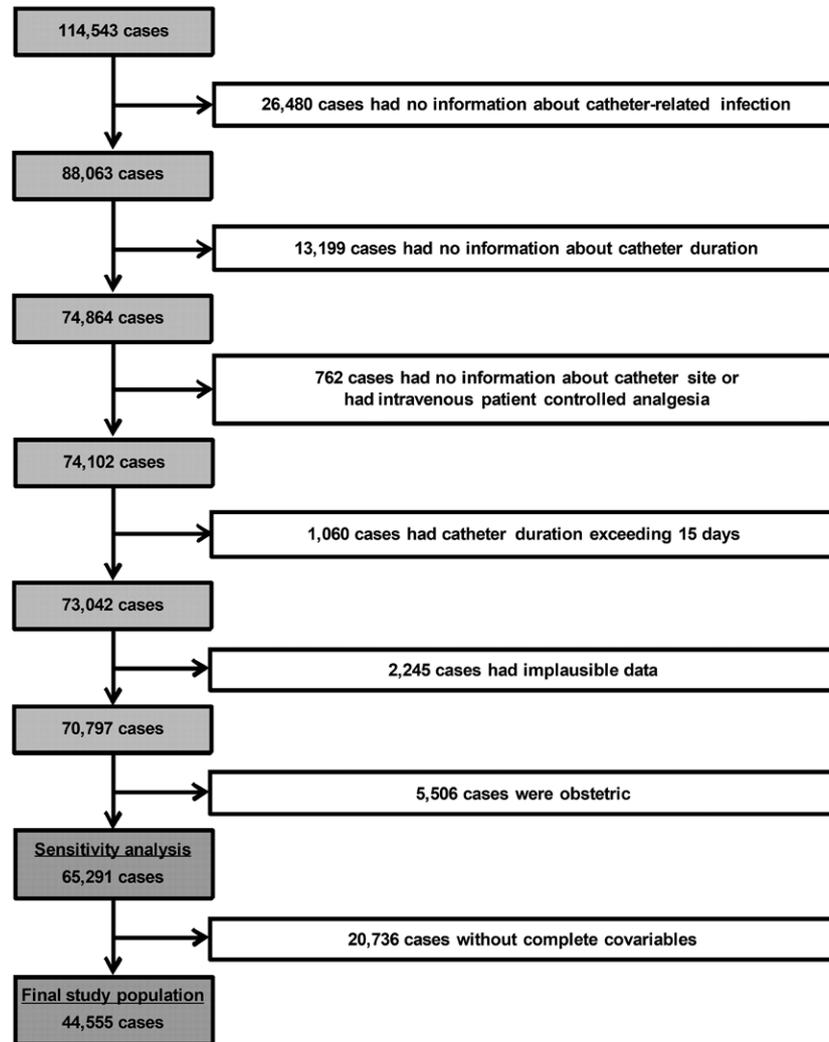


Fig. 1. Case selection.

from likelihood ratio test statistics. Additionally, the  $-2$  log likelihood of final covariate model is given. As a sensitivity analysis, we also estimated a Kaplan–Meier survival curve in a larger study population that contained details about catheter duration and infection, but incomplete covariables (fig. 1).

Data analysis was performed using IBM SPSS Statistics for Windows, version 19 (IBM). Continuous variables are expressed as means and SDs. Categorical variables are presented as absolute and relative frequencies, respectively. Two-sided  $P$  values 0.05 or less were considered statistically significant.

## Results

There were 65,291 patients with continuous nerve blocks and information about catheter duration and infection (sensitivity analysis). A total of 44,555 of these patients had complete covariable data (fig. 1), which are specified in tables 1 and 2 (final study population). Our analysis is based on a total of 693 peripheral nerve catheter infections and 804 epidural catheter infections.

Among 24,103 patients with peripheral catheters, 941 were less than 18 yr old (6 cases with infection), and 153 were less than 12 yr old (1 case with infection). Among 20,452 patients with epidural catheters, 387 were less than 18 yr old (16 cases with infection) and 90 were less than 12 yr old (5 cases with infection).

### Peripheral Catheters

Characteristics of the patients with complete data about covariables are presented in table 1. Patients without infection were younger, more likely to be female, and less likely to have comorbidities. Patients without infection were also more likely to have surgery in traumatology and orthopedics and more likely to receive psoas blocks. Clear differences with absolute standardized differences ( $> 0.2$ ) between the groups were found for BMI (absolute standardized differences, 0.33), diabetes (absolute standardized differences, 0.22), surgical department (absolute standardized differences, 0.68), femoral site (absolute standardized differences, 0.27), and psoas site (absolute standardized differences, 0.46).

**Table 1.** Peripheral Catheter, Population Characteristics

	No Infection (n = 23,410)	Infection (n = 693)	ASD*
Age (yr)	57 ± 19	60 ± 16	0.16
Male	11,170 (48)	363 (52)	0.09
Body mass index (kg/m <sup>2</sup> )	28 ± 6	30 ± 7	0.33
ASA physical status ≥ II	19,473 (83)	622 (90)	0.18
Diabetes	3,194 (14)	161 (23)	0.28
Traumatology and orthopedics	17,782 (76)	323 (47)	0.68
Other departments	5,628 (24)	370 (53)	0.68
Peripheral catheters			
Interscalene	5,361 (23)	145 (21)	0.05
Infraclavicular	649 (3)	25 (4)	0.05
Axillary	258 (1)	7 (1)	0.01
Femoral	6,279 (27)	270 (39)	0.27
Sciatic nerve	5,496 (23)	216 (31)	0.18
Psoas catheters	5,135 (22)	22 (3)	0.46
Others	232 (1)	8 (1)	0.02
Multiple skin puncture	1,986 (8)	66 (10)	0.04

Continuous variables are expressed as means ± SDs and categorical variables as no. (%). Other surgical specialties include vascular surgery, pediatric surgery, cardiac surgery, and neurosurgery. Other peripheral catheters include supraclavicular, suprascapular, and saphenous nerve.

\*Absolute standardized differences (ASD) are the absolute values of difference in means or proportions (infection-free catheter use minus catheter-related infection) divided by the pooled SD.

ASA = American Society of Anesthesiologists.

**Table 2.** Epidural Catheter, Population Characteristics

	No Infection (n = 19,648)	Infection (n = 804)	ASD*
Age (yr)	61 ± 16	60 ± 15	0.06
Male	10,147 (52)	455 (57)	0.10
Body mass index (kg/m <sup>2</sup> )	27 ± 6	27 ± 6	0
ASA physical status ≥ II	17,633 (90)	767 (95)	0.19
Diabetes	2,533 (13)	132 (16)	0.10
General surgery	4,928 (25)	263 (33)	0.18
Gynecology	1,624 (8)	40 (5)	0.12
Traumatology and orthopedics	6,196 (32)	90 (11)	0.44
Urology	3,929 (20)	140 (17)	0.06
Other departments	2,971 (15)	271 (34)	0.51
Epidural catheters			
Thoracic epidural	12,432 (63)	678 (84)	0.44
Lumbar epidural	7,216 (37)	126 (16)	0.44
Multiple skin puncture	4,746 (24)	250 (31)	0.16

Continuous variables are expressed as means ± SDs and categorical variables as no. (%). Other surgical specialties include vascular surgery, pediatric surgery, and cardiac surgery.

\*Absolute standardized differences (ASD) are the absolute values of difference in means or proportions (infection-free catheter use minus catheter-related infection) divided by the pooled SD.

ASA = American Society of Anesthesiologists.

Before data exclusion, the incidence of infection in a larger patient cohort with incomplete information about catheter duration was 3.0% in 36,300 peripheral catheters. In the final study population, the incidence of peripheral catheter-related infections was 2.9% in 24,103 patients. The infection grade was mild in 593 cases (2.5%), moderate in 83 cases (0.3%), and severe in 17 cases (0.07%).

The probability of peripheral infection-free catheter use in patients with complete covariables was 98% at day 4 of catheter duration, 91% at day 7, and 57% at day 15 (fig. 2). With adjusted Cox regression analysis, the probability of peripheral infection-free catheter use was 99% at day 4 of catheter duration, 96% at day 7, and 73% at day 15 (fig. 3). Detailed information about the model is reported in Supplemental Digital Content 1A (<http://links.lww.com/ALN/B615>). The Kaplan–Meier survival curve calculated from a larger population lacking covariable details was generally similar (fig. 2, sensitivity analysis). In this larger population of 32,172 patients, 975 catheters were infected (3.0%).

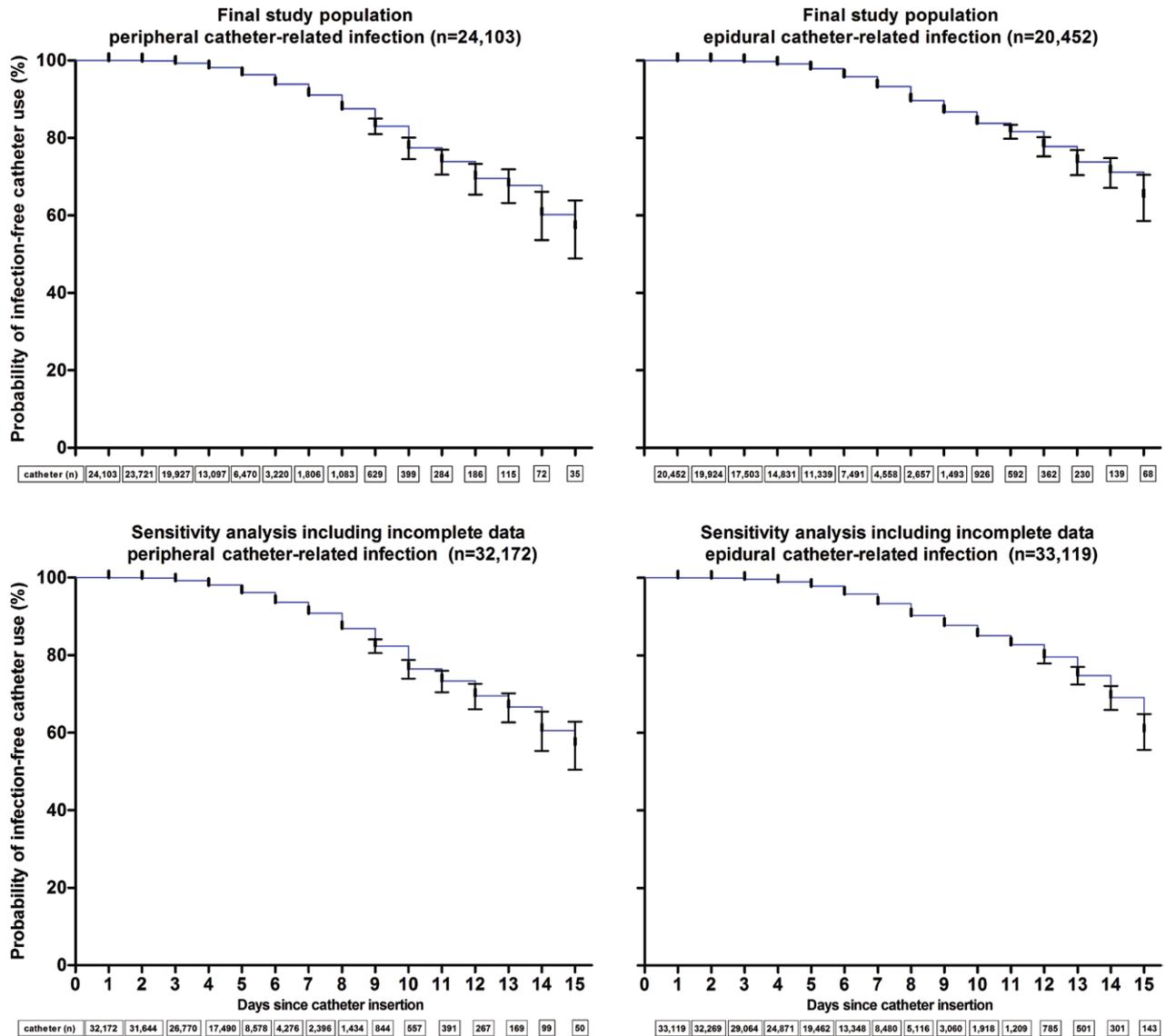
**Epidural Catheters**

Characteristics of the patients with complete information about covariables are presented in table 2. Patients without infection were more likely to be female and less likely to have comorbidities. Patients without infection were also more likely to have lumbar epidural catheters and more likely to have surgery in traumatology and orthopedics. They were also less likely to require multiple skin puncture. Clear differences with absolute standardized differences > 0.2 between the groups were found for traumatology and orthopedics (absolute standardized differences, 0.44), other surgical department (absolute standardized differences, 0.51), and thoracic epidural site (absolute standardized differences, 0.44).

Before data exclusion, the incidence of infection in a larger patient cohort with incomplete information about catheter duration was 3.9% in 43,568 epidural catheters. In the final study population, the incidence of epidural catheter-related infections was 3.9% in 20,452 patients. The grade of infection was mild in 676 cases (3.3%), moderate in 114 cases (0.6%), and severe in 14 cases (0.07%). The probability of epidural infection-free catheter use in patients with complete covariables was 99% at day 4 of catheter duration, 93% at day 7, and 65% at day 15 (fig. 2). With adjusted Cox regression analysis, the probability of epidural infection-free catheter use was 99% at day 4 of catheter duration, 95% at day 7, and 73% at day 15 (fig. 3). Detailed information about the model is reported in Supplemental Digital Content 1B (<http://links.lww.com/ALN/B615>). The Kaplan–Meier survival curve calculated from a larger population lacking covariable details was generally similar (fig. 2, sensitivity analysis). In this larger population of 33,119 patients, 1,441 catheters were infected (4.4%).

**Infection with Catheters Left In Situ**

In our final study population of 44,555 patients, 1,497 infected catheters were identified, of which 36 were left *in situ* (fig. 4). All 36 catheters progressed to higher infection grades. Twelve were peripheral and 19 were epidural; they initially showed mild signs of infection after 5.2 ± 2.4 (range, 1 to 10) days and progressed to moderate infection after an additional 1.7 ± 1.8 (0.5 to 8) days. The remaining five cases (three lumbar and two thoracic epidural catheters) initially showed mild or moderate signs of infection after 5.2 ± 2.8 (3 to 10) days



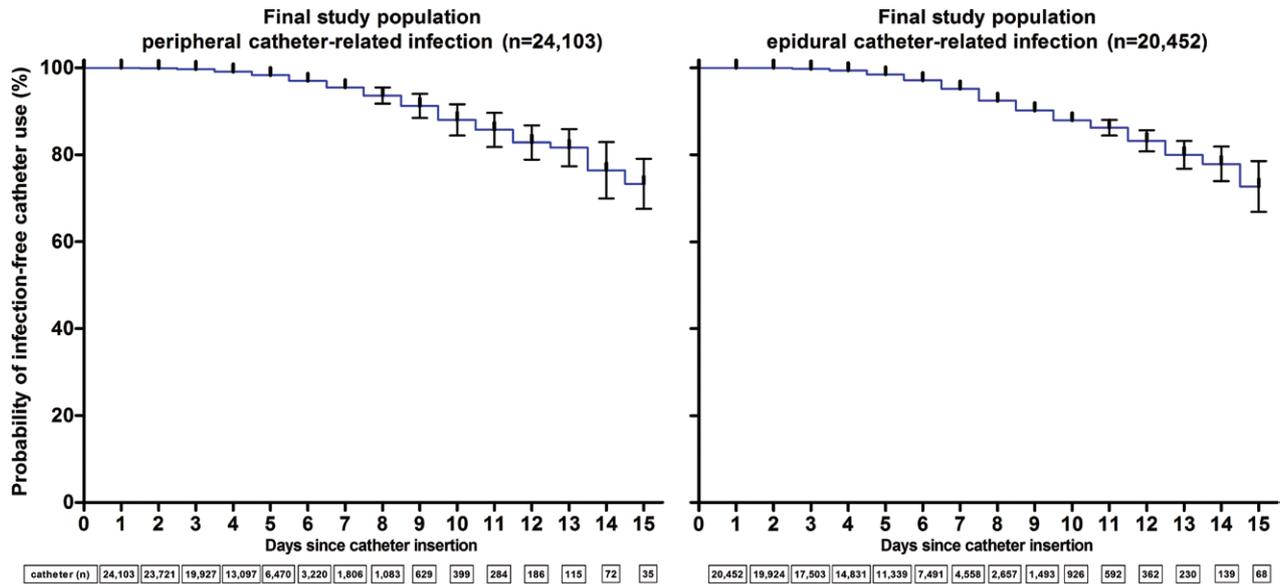
**Fig. 2.** Kaplan–Meier survival plots for catheter use over 15 days and the probability of infection-free catheter use. Censoring was considered, and Kaplan–Meier survival rates along with respective 95% CIs are presented. *Bold black dashes:* sign for censored data. *Black error bar:* 95% CI. Final study population had a complete set of covariates: data include validate information of infection, catheter duration, site, year of surgery, hospital center, and all variables listed in tables 1 and 2. Sensitivity analyses include the primary cohort not necessarily with a complete set of covariates: data include validated information of infection, catheter duration, and site.

and progressed to severe infection after an additional  $1.6 \pm 0.6$  (1 to 2) days that prompted surgical intervention.

### Discussion

Each additional day of catheter use, starting on the fourth day after insertion, was strongly associated with an increased risk of catheter-related infection for both peripheral and epidural catheters. Previous studies also identify prolonged catheter use as a risk factor for infection,<sup>6–9</sup> but our multi-center results enhance current understanding by specifically evaluating infection risk as a function of catheter duration. The fact that infection risk increases over time is consistent with experience with central venous catheters.<sup>26,27</sup>

The overall incidence of peripheral catheter–related infections was 2.9% in our study, which is higher than previously reported.<sup>9,13–15</sup> The 3.9% incidence of nonobstetrical epidural catheter–related infections was higher than in previous reports.<sup>6</sup> However, also, the probability of infection-free catheter use was 99% at day 4 for both peripheral and epidural catheters. It is likely that our incidence was higher because our maximum catheter duration was 15 days, which is longer than in previous studies.<sup>6,9,13–15</sup> In previous studies, an increased incidence of catheter-related infection in trauma patients was observed.<sup>7,9,15</sup> In these studies, trauma patients had a prolonged intensive care unit stay, which was identified as an independent risk factor for



**Fig. 3.** Cox regression survival plots for catheter use over 15 days and the probability of infection-free catheter use. Data are shown censored and with 95% CIs. **Bold black dashes:** sign for censored data. **Black error bar:** 95% CI. Final study population had complete covariables: data include validate information of infection, catheter duration, site, year of surgery, hospital center, and all variables listed in tables 1 and 2. Cox regression analyses were adjusted for age, sex, body mass index, American Society of Anesthesiologists physical status, diabetes, surgical specialty, catheter site, multiple skin puncture, year of surgery, and hospital center.

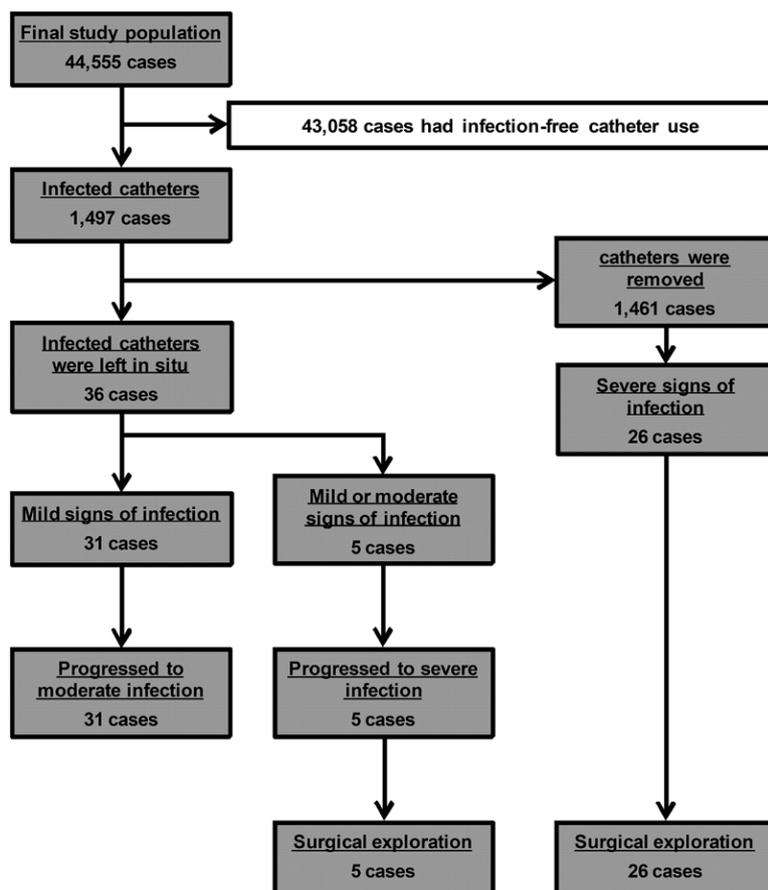
catheter-related infections. In contrast, our trauma/orthopedic patients mainly had elective surgery without intensive care unit stays. There were also differences in definitions of infection and inflammation, patient population, preventive hygiene measures, and probably many unknown factors. A strength of our study is a clear *a priori* definition of the criteria for infection, which was lacking in some previous investigations.

In most cases, only mild signs of infection (redness, swelling, or local pain) were observed—presumably because catheter insertion sites were inspected daily and catheters were usually removed when signs of infection were first detected. Infected catheters that were left *in situ* progressed to higher infection grades. Our results thus suggest that catheter insertion sites should be inspected daily because the time interval between the onset of symptoms and infection progression is usually less than 48 h. Among 36 patients with initial signs of mild or moderate infection in whom the catheter was left *in situ*, five developed severe infection requiring surgical exploration. Interestingly, in our final study population of 44,555 patients, we observed only 31 cases (0.07%) with severe infection and prompt surgical exploration. Catheters were removed with the first observed sign of local infection in 26 of these 31 cases. However, progression could presumably have been avoided in five cases in which the catheter was left *in situ* with initial mild or moderate signs of infection. This observation is consistent with previous studies about infection of body-foreign material *in situ* including cardiovascular implantable electronic devices.<sup>28</sup> We therefore recommend removing infected catheters immediately.

Several different risk factors for catheter-related infection have been identified: American Society of Anesthesiologists physical status, diabetes, type of surgery, catheter site, multiple skin puncture, and BMI.<sup>6,7,9,11,12,15,24,25,29–31</sup> All were included as confounders in our Cox regression analysis.

Our analysis was limited to the risk of catheter-related infection for peripheral and epidural catheters. We do not have sufficient information about the method of treatment, longer-term recovery, duration of hospitalization, or mortality. Consequently, we cannot determine whether the observed infections were linked to more serious outcomes. Moreover, some confounders with potential influence on catheter-related infection are missing in our analysis, including severity of diabetes, stage of cancer, grade of renal failure, redo surgery, and amount of steroid use or other immunosuppressive medication.

Our clinically routine documentation was electronically transferred into the registry. Since the registry design was pragmatic, the level of documentation varies from center to center. Many cases were thus excluded because of missing information about duration of the catheter and infection. The high number of excluded patients increases the risk of bias in our analysis. Nevertheless, we included 65,291 cases in our primary cohort, all with continuous nerve blocks and information about catheter duration and infection. This population was reduced to 44,555 cases, all with complete covariables. However, univariable results from all relevant patients (n = 65,291) were generally similar to both univariable and adjusted results using a multiple regression approach in



**Fig. 4.** Flow chart of infection with catheters that were left *in situ*. Mild infections were defined by at least two of three infection signs (redness, swelling, or local pain); moderate infections were defined as mild in addition to at least one of the following findings: increased C-reactive protein, leucocytosis, fever, or pus at the punctured site; and severe infections were defined by the need for a surgical incision or revision.

patients with all available information ( $n = 44,555$ ), suggesting data were missing completely at random and did not introduce substantial bias. As in any nonrandomized analysis, residual confounding may invoke error which cannot be eliminated in the framework of our sensitivity analysis.

During the seven-year 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. 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 an *a priori* definition.

In summary, the risk of peripheral and epidural catheter-related infection substantially increases over time. When catheters develop signs of infection, attention is needed to avoid progress of infection.

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## Competing Interests

The authors declare no competing interests.

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## Appendix 1: Recorded Items of the German Network for Regional Anesthesia

### Items for Block Procedure/Catheter Placement

Clinical department  
Ward  
American Society of Anesthesiologists physical status  
Sex  
Age  
Weight  
Height  
Operation and procedures code (German modification of the International Classification of Procedures in Medicine)  
Type of surgery  
Chronic pain patient  
Opioid use longer than 1 month  
Preoperative pain level at rest and on exertion  
Renal function  
Diabetes  
Peripheral arterial occlusive disease  
Rheumatoid arthritis  
Alcohol abuse  
Drug abuse  
Liver insufficiency (greater than Child–Pugh score B)<sup>32–34</sup>  
Immune deficiency  
Steroid use  
Other immunosuppressive drugs  
Transplanted organs  
Sepsis or presence of systemic infection  
Antibiotic therapy or prophylaxis  
Anticoagulant drugs according to guideline

Patient status awake, sedated (opioid, benzodiazepine, other), general anesthesia, block in an anesthetized area  
Multiple skin penetration  
Sterile standards (gown, tunneling, filter, suture)  
Bloody tap, unintended dura puncture, pneumothorax, intoxication  
Block abandoned for anatomical reasons or patient's wish  
Use of sonography (quality of visualization and of local anesthetic distribution)  
Needle type  
Drugs given  
Unplanned additional analgesia necessary (including general anesthesia if block fails)  
Loss of resistance with air, sodium chloride solution, or hanging drop  
Unintended paresthesia

### Items for Catheter Visits

Patient identification, date, time, duration  
Regular or irregular catheter removal  
Anticoagulation status at the time of removal according to guidelines  
Mobilization scale, sedation scale  
Satisfaction with pain therapy  
Presence of transient neurologic symptoms, headache after dural puncture hematoma, neuropathic pain, blood patch  
Pain levels (Numeric Pain Rating Scale [NRS]\*) at rest and on exertion within the expected area of effective regional analgesia  
Pain level of whole body (NRS)  
Muscle strength (six-point system according to Janda with 0 = inability of a contraction, 1 = detectable contraction, 2 = movements possible but not against gravity, 3 = against gravity, 4 = against moderate resistance, 5 = full muscle strength)  
Hypoesthesia, paresthesia  
Pain interference with mobilization, respiration, sleep  
Coanalgesics  
Treatment necessity for urinary retention, respiratory depression, nausea, vomiting, pruritus  
Catheter-associated hypotension  
Catheter manipulations, site-specific alterations like occlusions, leaks, technical problems  
Grade of catheter-related infection  
Infusion rate, boli, lockout times  
\*NRS is a numeric version of the visual analog scale in which a respondent selects a whole number (0 to 10). The scale ranges from 0, "no pain," to 10, "worst pain."<sup>35,36</sup>

## Appendix 2: Study Protocol

### 1. Hypothesis

We hypothesized that each additional day of catheter use is associated with an increased risk of catheter-related infection.

## 2. Outcome Definition

The primary outcome was a composite of the presence of a mild, moderate, or severe catheter-related infection up to 15 days. The secondary outcome was progression of low-grade (mild/moderate) infection of catheters left *in situ* to higher-grade (moderate/severe) infections.

## 3. Inclusion/Exclusion Criteria

Inclusion criteria for the final study population were patients 0 to 100 yr old who had peripheral or epidural catheters inserted for surgical procedures, information about catheter *in situ* time, information about catheter-related infection, sex, BMI, American Society of Anesthesiologists physical status, diabetes, surgical specialty, multiple skin puncture, year of surgery, and hospital center. Exclusion criteria were defined as catheter duration for more than 15 days, catheter used for obstetric analgesia, and implausible data.

## 4. Proof of Plausibility

Table A2.1

Items in the Registry	Indications of Implausible Data
Day of catheter placement	Implausible if catheter placement takes place before date of birth or after catheter removal
Catheter <i>in situ</i> time	Implausible if time between catheter placement and removal differs from catheter <i>in situ</i> time
Catheter-related infection	Implausible if catheter-related infection is documented before catheter placement
Date of ward round	Implausible if ward round is documented before catheter placement
Age	Implausible if catheter placement takes place before date of birth Implausible if patient for pediatric surgery is older than 18 yr Implausible if age and body height are not consistent (e.g., age: 2 yr, height: 180 cm) Implausible if age and body weight are not consistent (e.g., age: 2 yr, weight: 80 kg) Implausible if age is less than 0 or more than 100
Male	Implausible if patient for obstetrics is male
Body mass index	Implausible if body height and body weight are not consistent (e.g., height: 180 cm, weight: 10 kg)
Diabetes	Implausible if American Society of Anesthesiologists physical status is I
Peripheral catheters	Implausible if catheter site is described as intrathecal, thoracic, or lumbar
Epidural catheters	Implausible if catheter site is described as intrathecal, peripheral, or the use of nerve stimulation

## 5. Missing Data Handling/Subgroup Sensitivity Analysis

A sensitivity analysis was planned in a larger cohort of patients with continuous nerve block, information about catheter duration, catheter-related infection, and incomplete

covariables (age, sex, BMI, American Society of Anesthesiologists physical status, diabetes, surgical specialty, multiple skin puncture, year of surgery, and hospital center).

*Post hoc* sensitivity analysis was performed in a larger patient cohort with information about catheter-related infection and catheter site only.

## 6. Statistical Analysis

Absolute standardized differences to describe population characteristics between the groups were defined *a priori*. Kaplan–Meier survival curves and Cox regression analyses were planned *post hoc*.

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