Diabetes
A Risk Factor for Catheter-Associated Infections

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Background and Objectives: The incidence of infectious complications associated with continuous regional anesthesia techniques is a matter of concern. Our objective was to determine whether patients suffering from diabetes are at an increased risk of catheter-related infectious complications.

Methods: The German Network for Regional Anaesthesia database was analyzed between 2007 and 2012. After proof of plausibility, data of 36,881 patients undergoing continuous regional anesthesia were grouped in I: no diabetes (n = 32,891) and II: any diabetes (n = 3990). The analysis focused on catheter-related infections after strict definition. Differences among the groups were tested with t and χ^2 tests. Odds ratios were calculated with logistic regression and adjusted for potential confounders.

Results: Patients with a diagnosis of diabetes had an increased incidence of catheter-related infections (no diabetes 3.0% vs any diabetes 4.2%; $P < 0.001$). Among all patients, diabetes remained an independent risk factor for infections for all sites after the adjustment for potential confounders (odds ratio [OR] = 1.26; 95% confidence interval [95% CI], 1.02–1.55; $P = 0.036$). The risk of infection was significantly increased in peripheral catheters only in the lower limb (adjusted OR = 2.42; 95% CI, 1.05–5.57; $P = 0.039$). If neuraxial catheters were used, the risk was significantly increased only in lumbar epidural (adjusted OR = 2.09; 95% CI, 1.18–3.73; $P = 0.012$) for diabetic patients compared with nondiabetic patients.

Conclusions: The presence of diabetes is associated with an increased risk for catheter-related infections in lower limb and lumbar epidural. Specific care should be taken to avoid and detect infections in this population.

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The overall incidence of catheter-related infections of continuous regional anesthesia has been found to range from 0% to 3%[1] depending on the catheter location. Single-center studies found lower infection rates for interscalene (0.9%) and popliteal catheters (0.2%–0.9%)[2,3] compared with axillary and infraclavicular catheters (3%–7%).[4]

The rate of infections after epidural catheter placement has been estimated from 0.8% to 3.0%.[5–7] Severe infections like epidural abscess formation are approximated between 0.00% and 0.05%.[7–9] Discrepancies may be caused by the definition of infection and inflammation, size of patient population, disinfectant agent use, preventive hygiene measures, and probably many unknown factors.

In the past 30 years, the incidence of diabetes has been rising worldwide.[10] According to latest estimates by Guariguata et al,[11] the worldwide incidence of diabetes will continue to increase until 2035. In Germany, diabetes mellitus is a widespread disease with an increasing prevalence.[11] In 2000, 6.5% of the German population suffered from diabetes mellitus, whereas in 2009, the number of patients increased to approximately 9.7%.[12–14] A recent study reports about a diabetes prevalence of 11.9% in Germany.[11]

Diabetes is known to compromise the efficiency of the immune system.[15] Diabetes is a known independent risk factor for catheter-related bloodstream infections.[16] However, it still remains unclear if diabetes is also an independent risk factor for infectious complications of regional anesthesia catheter use.[1]

In 2007, the German Society for Anesthesiology and Intensive Care Medicine established a network for safety in regional anesthesia. Data describing the state of health of each patient, type and localization of regional anesthesia procedure, and potential complications during treatment and catheter use were collected in a registry.

Therefore, we decided to study the effects of diabetes on catheter-associated infections defined within the German Network for Regional Anaesthesia (NRA) database.

METHODS

Data from the NRA were analyzed from September 2007 to November 2012. Twenty-five clinical centers in Germany participated in the data collection. The data analysis was conducted at Saarland University Medical Centre, Germany. The analysis of anonymized data was approved by the ethics committee (Ärztekammer Saarland No. Ha50/11). The approval did not require written consent because the data were anonymous

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Structure of the Network

The NRA database collects preoperative, intraoperative, and postoperative data by treating physicians by means of standard form documentation. The NRA documentation provides detailed information about health conditions of the patients undergoing a regional anesthesia procedure (personal data and comorbidities), regional anesthesia procedures including details of catheter setup, and the postoperative course evaluated during daily ward rounds until the day after catheters are removed. The data collection was carried out in the context of regular patient treatments and standard file administration of the respective hospital, whereby IT services provided the opportunity to transfer the collected data anonymously via interfaces between the hospital and the collecting server. The structured export of data is performed by a manual upload of an https-encrypted XML file without storage of data directly identifying individuals like names and birth date. The stream of data ended in an Internet-accessible database, which had been ensured with special safety provisions.

Definition of Infection

Definitions of varying degrees of infection were developed in a Delphi consensus process.[17]

Mild infection: presence of 2 symptoms out of redness, swelling, and pain.

Moderate infection: mild infection plus 2 criteria: increased C-reactive protein, leukocytosis, fever, or pus at the punctured site.

Severe infection: necessity of a surgical intervention such as incisions or revisions.

Validation of Data

The database included 217,087 data sets in the abovementioned period. We initially assessed the face validity of the database's diabetes type codes by comparing with the frequency of diabetes in a reference population (10.8% vs 9.7%[14]). We identified 67,657 procedures with any grade of infection. Before dividing the data into groups, they were validated according to specific rules. Reasons for deletions were missing ID, missing the prolonged catheter duration, single shot blocks, intravenous patient-controlled analgesia, multiple appearances of the cases, no information about infections, missing gender, missing age, missing weight, missing catheter site, and missing entries to diabetes. These deletions result in the final study population of 36,881 cases, all with continuous regional anesthesia catheters (Fig. 1). Based on low cases, the localizations paravertebral, combined spinal-epidural anaesthesia, psoas compartment, and intrathecal were summarized to the variable "other neuraxial catheters."

Study Population

The final study cohort consisted of 36,881 cases and was subdivided into the following groups: nondiabetic (ND) cases (n = 32,891) and diabetic (D) cases (n = 3990).

End Points

The primary end point of the study was any grade of infection depending on diabetic disease. Secondary end point was the grade of infection (mild, moderate, and severe) depending on catheter site.

Statistical Analysis

All selected variables for the present analysis from the NRA database are reported in Tables 1 and 2. Continuous variables were expressed as mean and SD. Categorical variables were presented in percentage, unless otherwise stated.

Chi-square tests were performed for the comparison of frequencies between groups and were followed by Fisher exact test if necessary. For continuous variables, the differences between groups were compared using Student *t* tests (respectively, Welch *t* tests in case of inhomogeneous variances). Statistical significance was accepted at $P \leq 0.05$.

Logistic regression analysis was used to calculate univariate and multivariate odds ratios (ORs) with 95% confidence intervals (95% CIs). Potential confounders were gender, age, body mass index, antibiotic prophylaxis, multiple skin puncture, and prolonged catheter duration of 4 days or longer. Collinearity was tested by Pearson, respectively, Spearman correlation coefficients. Variables with a positive correlation greater than 0.3 were excluded. The goodness of fit was assessed by Hosmer-Lemeshow tests; all tests were not statistically significant.

All variables were verified with center analyses to avoid center effects. For each center, frequency analyses were performed and OR and 95% CIs were calculated by logistic regression. All data analyses were performed using SPSS Statistics version 19 (IBM, Armonk, NY).

RESULTS

Table 1 provides general information about the characteristics of patients who received regional anesthesia catheter placement. Among nondiabetic patients, there were more women, they were younger and had a lower body mass index, and antibiotic prophylaxis was less frequently used compared with diabetic patients. In nondiabetic patients, more lumbar epidural procedures were performed in comparison with diabetic patients. The rates of multiple skin puncture and the prolonged catheter duration were lower in nondiabetic patients compared with diabetic patients.

Site-Dependent Infections

Nondiabetic patients had a significantly lower incidence of any grade of infection compared with diabetic patients (ND, 3.0% vs D, 4.2%; $P < 0.001$). Also, the incidence of mild (ND, 2.4% vs D, 3.0%; $P = 0.008$) and moderate infections (ND, 0.5% vs D, 1.0%; $P = 0.001$) was significantly lower. Interestingly, severe infections were twice as high among patients with diabetes although not significantly different (ND, 0.1%; D, 0.2%; $P = 0.27$).

The incidence of infection of diabetic patients was increased for any location, except the thoracic epidural location, in which the incidence of infection was comparable (ND, 5.2%; D, 5.2%; $P = 1$; Table 2). However, significant differences in peripheral sites were only observed for the lower limb (any grade of infection: ND, 2.7% vs D, 3.9%; $P = 0.03$), whereas in detail only for moderate infection (ND, 0.4 vs D, 1.3; $P = 0.001$). Significant differences in neuraxial sites between the groups were observed for lumbar epidural procedures (any grade of infection: ND, 2.0% vs D, 7.0%; $P < 0.001$); in detail: mild (ND, 1.1% vs D, 2.9%; $P = 0.002$) and moderate (ND, 0.8% vs D, 3.7%; $P < 0.001$; Table 2).

Influencing Factors for Catheter-Related Infections

Confounders that increase the risk for catheter-related infections were prolonged catheter duration of 4 days or longer, multiple skin puncture, body mass index, and age (Table 3). In contrast, antibiotic prophylaxis and female gender decrease the risk for catheter-related infections.

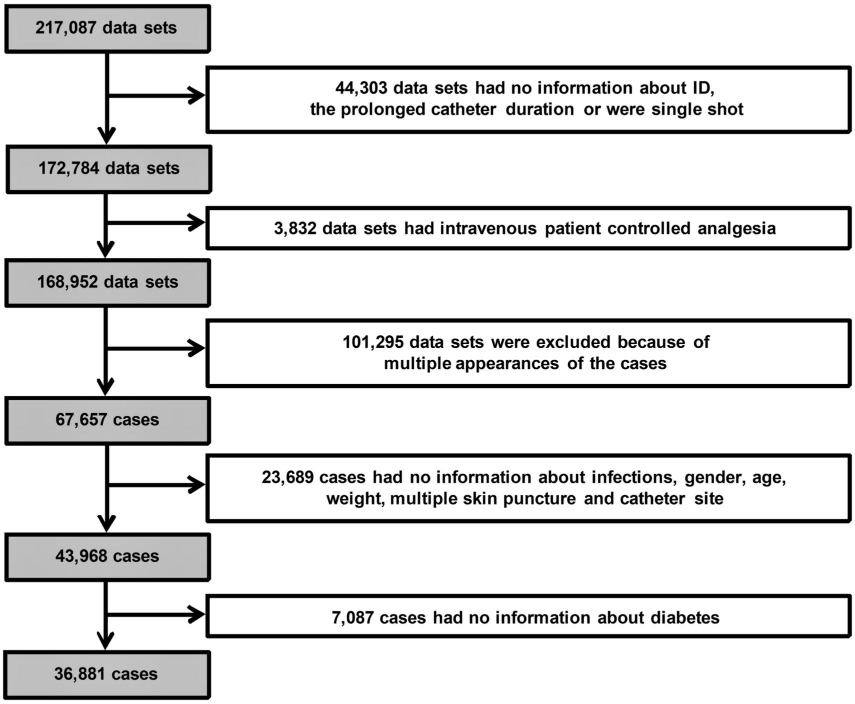

FIGURE 1. Flow chart of data selection.

Diabetes as Risk Factor for Catheter-Related Infections

Among all patients and all catheter sites, diabetes remained an independent risk factor for the incidence of infection after the adjustment for potential confounders (OR = 1.26; 95% CI, 1.02–1.55; $P = 0.036$; Table 3).

Interestingly, in peripheral catheters, diabetes remained an independent risk factor for infections after the adjustment for potential confounders only in lower limb and only for moderate infections (OR = 2.42; 95% CI, 1.05–5.57; $P = 0.039$; Table 4).

In neuraxial catheters, diabetes remained an independent risk factor for infections after the adjustment for potential confounders only in lumbar epidural catheters, for any grade of infections

TABLE 1. Population Characteristics

	No Diabetes (n = 32,891)	Any Diabetes (n = 3990)	*P*
Demographics			
Female, %	19,623 (60)	1988 (50)	<0.001*
Age (mean ± SD), y	52.9 ± 19.6	65.6 ± 3.5	<0.001*
BMI (mean ± SD), kg/m^2	27.1 ± 5.6	30.1 ± 6.1	<0.001*
ASA score (mean ± SD)	2.2 ± 0.7	2.7 ± 0.6	<0.001*
Antibiotic prophylaxis, %	19,334 (59)	2615 (66)	<0.001*
Catheter sites			
Upper limb, %	4716 (14)	533 (13)	0.13
Lower limb, %	6738 (21)	1000 (25)	<0.001*
Thoracic epidural, %	9246 (28)	1294 (32)	<0.001*
Lumbar epidural, %	6904 (21)	487 (12)	<0.001*
Other neuraxial catheters, %	5287 (16)	676 (18)	0.14
Catheter			
Multiple skin puncture, %	6092 (19)	872 (22)	<0.001*
Prolonged catheter duration ≥4 days, %	16,965 (52)	2503 (63)	<0.001*

Upper limb: axillary, infraclavicular, supraclavicular, suprascapular, interscalene. Lower limb: femoral, sciatic nerve, saphenous nerve. Other neuraxial catheters: paravertebral, combined spinal-epidural anesthesia, psoas compartment, intrathecal. BMI: body mass index. ASA: American Society of Anesthesiologists physical status score. SD: standard deviation. Values $P < 0.05$ were considered as statistically significant.

TABLE 2. Number of Infections

	No Diabetes (n = 32,891)	Any Diabetes (n = 3990)	*P*
All sites, %	982 (3.0)	167 (4.2)	<0.001*
Mild	779 (2.4)	122 (3.0)	0.008*
Moderate	174 (0.5)	39 (1.0)	0.001*
Severe	29 (0.1)	6 (0.2)	0.27
Upper limb, %	173 (3.7)	24 (4.6)	0.34
Mild	138 (2.9)	19 (3.6)	0.42
Moderate	32 (0.7)	4 (0.8)	0.78
Severe	3 (0.1)	1 (0.2)	0.35
Lower limb, %	177 (2.7)	39 (3.9)	0.03*
Mild	145 (2.2)	24 (2.4)	0.64
Moderate	27 (0.4)	13 (1.3)	0.001*
Severe	5 (0.1)	2 (0.2)	0.23
Thoracic epidural, %	478 (5.2)	67 (5.2)	1
Mild	406 (4.4)	63 (4.9)	0.43
Moderate	60 (0.7)	3 (0.2)	0.08
Severe	12 (0.1)	1 (0.1)	1
Lumbar epidural, %	137 (2.0)	34 (7.0)	<0.001*
Mild	75 (1.1)	14 (2.9)	0.002*
Moderate	53 (0.8)	18 (3.7)	<0.001*
Severe	9 (0.1)	2 (0.4)	0.16

(OR = 2.09; 95% CI, 1.18–3.73; *P* = 0.012), as well as for mild (OR = 2.25; 95% CI, 1.01–5.03; *P* = 0.049) and moderate grade of infection (OR = 2.32; 95% CI, 1.32–4.08; *P* = 0.003).

DISCUSSION

In the present multicenter register analysis of 36,881 patients, diabetes was strongly associated with catheter-related infections. It is the first study to show that the incidence of infection was increased in all catheter sites in diabetic patients compared with nondiabetic patients, except for the thoracic epidural site. This was true for each grade of infection. However, after adjustment for potential confounders, diabetes remained an independent risk factor for catheter-related infections compared with nondiabetic patients only for catheters of the lower limb (moderate grade of infection: OR = 2.42; 95% CI, 1.05–5.57; *P* = 0.039) and for lumbar epidural catheters (any grade of infection: OR = 2.09; 95% CI, 1.18–3.73; *P* = 0.012).

Regional anesthesia leads to reduced postoperative morbidity and mortality.[18–21] Analgesia for prolonged times can be accomplished using catheter techniques. However, catheter-related infections are common. Therefore, identification of patients having an increased risk can be of great importance to avoid an infection. Until now, prolonged catheter duration, multiple skin puncture, obesity, diabetes, gender, and advanced age have been discussed controversially.[1,4,9,22–25]

Diabetic patients have an increased risk for catheter-associated infections. Additional risk factors like advanced age and prolonged catheter duration are described.[1,4,9,22,23] Furthermore, diabetes seems to be also associated with an increased risk for surgical site infections in general surgery.[26] Diabetes is a well-known risk factor for skin and soft tissue infections.[24]

Diabetes mellitus may impair tissue perfusion and wound healing and leads to higher rates of infection compared with nondiabetes.[27] Diabetes mellitus is associated with reduced response of T cells, neutrophil function, and disorders of humoral immunity.[27–29] Consequently, diabetes mellitus increases the susceptibility for catheter-associated infections.

In previous studies, advanced age was found as a risk factor for catheter-associated infections, however, only in the general population.[9,23] In our analysis, advanced age also had an increased risk. This can probably be caused by malnutrition, comorbidities, and immunosenescence.[30,31]

Previous studies found that catheter-associated infections in the general population were increased in the thoracic location compared with the lumbar location.[8,9] That is in line with our results in the general population but contrasts our findings in diabetic patients. After the adjustment for potential confounders, diabetic patients had an increased risk for infections of the lumbar epidural location. The density of perspiration glands is higher in the skin of the lumbar site, as is the tendency of patients lying in bed to perspire in this area. This action creates a microenvironment that fosters bacterial retention and growth in the lumbar area. Skin infection of diabetic patients seems to be associated with *Staphylococcus aureus*, group B streptococci, anaerobes, and gram-negative bacilli.[24]

Therefore, skin hygiene of the lumbar site seems to be of great importance to minimize catheter-related infection in diabetic patients.

The strongest risk factor for catheter-associated infections in the general population is prolonged catheter duration.[1,4,9,22,23] Accordingly, catheter use of 4 days or longer was the strongest

TABLE 3. Influencing Factors for Catheter-Related Infections in All Patients

	All Patients (n = 36,881) Odds Ratio	95% CI	*P*
Diabetes	1.26	1.02–1.55	0.036*
Female	0.71	0.61–0.82	<0.001*
Age	1.01	1.01–1.02	<0.001*
Body mass index	1.01	1.01–1.03	0.031*
Antibiotic prophylaxis	0.70	0.60–0.82	<0.001*
Multiple skin puncture	1.43	1.20–1.71	<0.001*
Prolonged catheter duration ≥4 days	6.32	5.05–7.91	<0.001*

Data are expressed as odds ratios with 95% confidence interval (CI). Values of $P < 0.05$ were considered as statistically significant.

TABLE 4. Diabetes: A Risk Factor of Infection

All Patients (n = 36,881)		Odds Ratio	95% CI	*P*
All sites				
All	Crude	1.57*	1.28–1.92	<0.001*
	Adjusted	1.26*	1.02–1.55	0.036*
Mild	Crude	1.54*	1.22–1.94	<0.001*
	Adjusted	1.23	0.97–1.56	0.09
Moderate	Crude	1.70*	1.07–2.70	0.024*
	Adjusted	1.37	0.85–2.22	0.19
Severe	Crude	1.26	0.37–4.25	0.71
	Adjusted	1.13	0.32–3.97	0.85
Upper limb [%]				
All	Crude	1.32	0.80–2.16	0.28
	Adjusted	1.17	0.70–1.97	0.55
Mild	Crude	1.31	0.75–2.27	0.34
	Adjusted	1.20	0.67–2.14	0.54
Moderate	Crude	1.08	0.32–3.58	0.90
	Adjusted	0.89	0.26–3.04	0.85
Severe	Crude	4.49	0.41–49.66	0.22
	Adjusted	3.50	0.28–43.51	0.33
Lower limb [%]				
All	Crude	1.53*	1.03–2.28	0.035*
	Adjusted	1.18	0.78–1.78	0.45
Mild	Crude	1.27	0.79–2.03	0.32
	Adjusted	0.93	0.57–1.52	0.78
Moderate	Crude	2.87*	1.32–6.26	0.008*
	Adjusted	2.42*	1.05–5.57	0.039*
Severe	Crude	1.39	0.16–11.94	0.76
	Adjusted	1.97	0.19–20.26	0.57
Thoracic epidural [%]				
All	Crude	1.14	0.82–1.59	0.42
	Adjusted	1.19	0.85–1.67	0.31
Mild	Crude	1.29	0.92–1.81	0.14
	Adjusted	1.33	0.94–1.88	0.11
Moderate	Crude	0.39	0.09–1.62	0.20
	Adjusted	0.44	0.10–1.88	0.27
Severe	Crude	0.59	0.08–4.28	0.62
	Adjusted	0.49	0.06–3.82	0.50
Lumbar epidural [%]				
All	Crude	4.23*	2.48–7.23	<0.001*
	Adjusted	2.09*	1.18–3.73	0.012*
Mild	Crude	3.84*	1.83–8.07	<0.001*
	Adjusted	2.25*	1.01–5.03	0.049*
Moderate	Crude	4.98*	2.89–8.56	<0.001*
	Adjusted	2.32*	1.32–4.08	0.003*
Severe	Crude	3.17	0.68–14.70	0.14
	Adjusted	1.70	0.35–8.26	0.51

Data are expressed as odds ratios with 95% confidence interval (CI). Values of $P < 0.05$ were considered as statistically significant.

Adjusted for female, age, body mass index, antibiotic prophylaxis, multiple skin puncture, and prolonged catheter duration ≥4 days.

additional risk factor for catheter-associated infections in our analysis (OR = 6.32; 95% CI, 5.05–7.91; $P < 0.001$).

Few studies reported that the use of an antibiotic in the postoperative period can reduce the risk of local infection.[4,6] In addition, male gender seems to be significantly associated with an increased risk of local inflammation.[1] However, these statements were not clearly supported by power analyses. Nevertheless, in our analyses, we adjusted for gender and antibiotic prophylaxis as potential confounders.

Limitations

Our results imply an interaction between diabetes and catheter-associated infections, although the investigation was not primarily designed to clarify possible mechanisms of interaction. For further analyses and reliable explanation of interaction, metabolic parameters like blood glucose levels and HbA1c in the course of patients' hospital stay are desirable. Furthermore, current registry data do not provide information on long-term outcome of infections or mortality, which may also be a relevant modifiable risk factor and should be tested in further studies.

Because of our large total population, significant results can possibly be caused by the sample size. Nevertheless, a large total number of patients is necessary to report reliably about incidences of rare complications. A large register is especially important to screen for serious complications. During a long observation period of 5 years, progress in medicine, technique, or anesthesia methods possibly causes bias of the results and represents an important limitation of a register study. All medical centers participating in this registry are enthusiastic in the field of regional anesthesia. This can lead to bias in comparing our results with those of other studies.[7] Residual confounding represents a further limitation of a multicenter study.

Registries critically depend on the quality of data entry and handling. We cannot provide external validity. The distribution of diabetic patients, however, seems to be plausible.

Diabetic patients had an increased risk for catheter-associated infections compared with nondiabetic patients. Because these patients seem to be at an increased risk, glycemic control should come into the focus of patient management during their hospital stay. Further studies are needed to show that adequate glucose control is associated with fewer infections even in diabetic patients.

CONCLUSIONS

Diabetic patients had an increased risk for catheter-related infections compared with nondiabetic patients in lower limb and lumbar epidural location but not in upper limb and thoracic epidural location.

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