

## Clinical Outcomes and Risk Factors for Tunneled Hemodialysis Catheter-Related Bloodstream Infections

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Diabetes and left internal jugular vein insertion site were significantly associated with increased risk of a catheter-related bloodstream infection from a tunneled hemodialysis catheter. Ex-smoker status was significantly associated with reduced risk.

**Keywords:** catheter; hemodialysis; infection; vascular.

Challenges with timely permanent vascular access for hemodialysis (HD) lead to urgent insertion of tunneled catheters for hemodialysis (TCHD). In Australia, 15% of 10 624 prevalent HD patients were dialyzing via a central venous catheter in 2017 [1]. Catheter-related bloodstream infections (CRBSIs) from TCHD use occur at rates of 1.1–6.1 episodes per 1000 catheter-days internationally [2, 3]. CRBSI are associated with significant mortality, morbidity, and health care costs [4, 5]. To our knowledge, there are no published Australian data on patient factors associated with CRBSI. This study aimed to investigate factors associated with CRBSI in patients with a primary TCHD inserted at an Australian tertiary metropolitan hospital and report their microbiological and clinical outcomes.

### METHODS

The hospital's Human Research Ethics Committee approved the study (QA 021/19).

Patients with primary insertion of a TCHD from January 2013 to June 2018 were included. Patients were followed until the time of primary TCHD removal (documented in hospital records), death with a functioning TCHD, or December 31, 2018 (whichever came first). Patients were excluded if the primary

TCHD insertion was not within the study period, removal date could not be verified, or if the patient was not managed by the hospital's dialysis network. CRBSI episodes were identified using hospital admissions (ICD-10 AM code T82.7X assigned as principal or complicating discharge diagnoses) and the blood culture database. Patient demographics, comorbidities, and outcomes were extracted from admission notes. Insertions were performed by interventional radiologists using tunneled cuffed catheters (Palindrome chronic dialysis catheters, Medtronic, Minneapolis, MN, USA).

The control was primary TCHD not associated with CRBSI. CRBSIs were categorized as definite, probable, and possible according to the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines [6].

Categorical variables are reported as count and proportion, and continuous variables are summarized as median and interquartile range (IQR). Univariate logistic regression was used to compare cases with controls for each variable, and crude odds ratios (ORs), 95% confidence intervals (CIs), and 2-tailed *P* values were calculated. All variables with a *P* value <.1 in univariate analysis and variables identified a priori in the international literature as risk factors for CRBSI (age, diabetes, TCHD use for >90 days, hypertension [5, 7]) were included in the multivariate analysis regardless of univariate parameters. Multivariate logistic regression was used to identify independent demographic and clinical risk factors associated with CRBSI, with *P* values <.05 considered significant. Statistical analysis was performed using Stata 15.1 (StataCorp, College Station, TX, USA). Descriptive analyses of microbiological and clinical outcomes of CRBSI were performed.

### RESULTS

A total of 227 patients had a primary insertion of a TCHD. Table 1A summarizes patient demographics and comorbidities. Maintenance HD was performed for 4–5 hours, 3 times a week. Forty-two (19%) patients were on immunosuppressive therapy during the study period (steroid agent equivalent to ≥16 mg prednisone per day for >15 days or other immunosuppressive or immunomodulatory agent).

Of the 227 patients, 157 (69%) patients had a TCHD inserted for acute HD, and in 68 (30%) patients for maintenance renal replacement therapy (RRT) access failure, for example, mal-function or infection of either a peritoneal dialysis catheter or arterio-venous access. TCHD was removed in 45 (20%) patients who no longer required RRT, in 95 (42%) with established permanent RRT access, in 37 (16%) with proven or suspected TCHD infections, and in 19 (8%) with a nonfunctional TCHD. Fifteen (7%) patients died with a functioning TCHD. Reasons

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for removal, other than infection, could not be verified for 16 patients.

The aggregate rate was 1.28 CRBSIs per 1000 catheter-days. Thirty-nine primary TCHDs were associated with a CRBSI (17%). Twenty-four were defined as definite, 11 as probable, and 4 as possible according to the KDOQI guideline definitions [6].

In univariate analysis of CRBSI risk factors (Table 1A), there was no significant association with age, diabetes, days TCHD in situ, and hypertension. Ex-smoker status was associated with lower odds of CRBSI (OR, 0.32; 95% CI, 0.13–0.78), and insertion into the left internal jugular vein was associated with higher odds (OR, 3.91; 95% CI, 1.60–9.53). In multivariate analysis (Table 1B), diabetes (OR, 2.2; 95% CI, 1.02–4.75) and TCHD inserted into the left internal jugular vein (OR, 4.4; 95% CI, 1.65–11.72) were independently associated with increased risk of CRBSI. Ex-smoker status was independently associated with a reduced risk of CRBSI compared with nonsmokers (OR, 0.32; 95% CI, 0.13–0.80).

### Microbiology

There were 23 (59%) gram-positive bacteremias (4 methicillin-susceptible and 9 methicillin-resistant *Staphylococcus aureus*, 3 enterococci, and 7 coagulase-negative staphylococci), 10 (26%)

gram-negative bacteremias (2 *Pseudomonas aeruginosa*, 6 *Enterobacteriales*, and 2 environmental gram-negative organisms), 3 (8%) fungemias (2 *Candida* species, 1 *Cryptococcus neoformans*), and 3 (8%) were culture-negative.

### Infection Outcomes

Twenty-eight patients had a principal diagnosis of CRBSI on admission. The mean length of stay (LOS) was 14 days ( $\pm 12$  days). Eleven patients had a CRBSI occur as a complication during an inpatient admission with a mean LOS of 43 ( $\pm 21$ ) days following the onset of the CRBSI.

There were 2 (5%) in-hospital deaths, 1 (2.6%) episode of methicillin-susceptible *S. aureus* endocarditis, and 1 (2.6%) episode of *Candida* endophthalmitis. Seven (18%) cases had at least 1 subsequent CRBSI episode following the primary CRBSI. Eight (4%) controls had a CRBSI associated with a TCHD inserted after the primary TCHD.

### DISCUSSION

There was a total of 39 CRBSIs in 227 primary TCHD insertions (17%), requiring removal in 37 (16%) cases. Diabetes

**Table 1A. Patient Demographics and Comorbidities and Univariate Analysis of Risk Factors for CRBSI**

	CRBSI (n = 39)	No CRBSI (n = 188)	OR	Univariate 95% CI	P Value
Age, median (IQR), y	58 (42–69)	60 (51–70)	0.98	0.96–1.00	.072
Days catheter in, median (IQR)	73 (18–204)	95 (29–178)	1.00	0.997–1.00	.890
Catheter in >90 d, No. (%)	21 (54)	88 (47)	1.33	0.66–2.65	.424
Male, No. (%)	23 (16)	123 (20)	0.76	0.38–1.54	.445
Comorbidities					
Diabetic, No. (%)	21 (54)	79 (42)	1.61	0.80–3.22	.178
Hypertension, No. (%)	24 (1)	124 (66)	0.83	0.41–1.68	.598
Peripheral vascular disease, No. (%)	4 (10)	16 (9)	1.23	0.39–3.90	.727
Immunosuppressive, No. (%)	9 (23)	33 (18)	1.41	0.61–3.25	.42
Autoimmune, No. (%)	5 (13)	12 (6)	2.16	0.71–6.52	.173
Oncological, No. (%)	0	11 (6)	-	-	-
Smoking status					
Never smoked, No. (%)	25 (64)	85 (45)	1	-	-
Ex-smoker, No. (%)	7 (18)	75 (40)	0.32	0.13–0.78	.012
Current smoker, No. (%)	7 (18)	27 (14)	0.88	0.34–2.26	.79
Ethnicity					
Caucasian, No. (%)	30 (77)	146 (78)	1	-	-
Asian, No. (%)	2 (5)	24 (13)	0.41	0.09–1.81	.237
Aboriginal Australian and Torres Strait Islander	1 (3)	5 (3)	0.97	0.11–8.63	.981
Pacific Islander, No. (%)	4 (10)	7 (4)	2.78	0.77–10.10	.12
Other, No. (%)	2 (5)	5 (3)	1.95	0.36–10.51	.439
Satellite-metropolitan or regional dialysis center, No. (%)	11 (28)	49 (26)	1.11	0.52–2.41	.783
Insertion site					
Right internal jugular vein, No. (%)	29 (74)	170 (90)	1	-	-
Left internal jugular vein, No. (%)	10 (26)	15 (8)	3.91	1.60–9.53	.003
Femoral/other, No. (%)	3 (8)	0	-	-	-
Body mass index					
<25 kg/m <sup>2</sup> , No. (%)	13 (33)	71 (38)	1	-	-
25–29.99 kg/m <sup>2</sup> , No. (%)	2 (5)	14 (7)	0.78	0.16–3.85	.76
≥30 kg/m <sup>2</sup> , No. (%)	24 (62)	103 (55)	1.27	0.61–2.67	.523

**Table 1B. Multivariate Analysis of Risk Factors for CRBSI**

Variable	OR	95% CI	PValue
Left internal jugular vein	4.4	1.65–11.72	.003
Diabetes	2.2	1.02–4.75	.045
Ex-smoker	0.32	0.13–0.80	.015
Age, y	0.98	0.95–1.00	.096
Tunneled dialysis catheter in situ >90 d	1.24	0.58–2.66	.574
Hypertension	1.05	0.47–2.32	.908

Abbreviations: CI, confidence interval; CRBSI, catheter-related bloodstream infection; IQR, interquartile range; OR, odds ratio.

and left internal jugular vein insertion site were independent risk factors for CRBSI. Ex-smokers were less likely to acquire CRBSI.

Diabetics are more susceptible to infections, including CRBSI [7, 8]. A hyperglycemic environment may impair host responses, namely neutrophil chemotaxis, adhesion and intracellular killing, and humoral immunity, increasing the likelihood of infection [8]. This emphasizes the need to ensure that diabetic patients with renal impairment are carefully considered for timely permanent RRT access.

Of clinical note, TCHDs inserted into the left internal jugular vein were at an increased risk of CRBSI compared with the right. Forty-one (18%) primary TCHDs were inserted into the left internal jugular vein. Reasoning was not consistently documented; however, it can be hypothesized that the contralateral upper limb may have been preserved for arterio-venous access creation or that the preferred right internal jugular insertion site had inaccessible vascular anatomy. The left internal jugular vein insertion site has a longer and variable anatomical course to the right atrium compared with the right internal jugular vein. This larger surface area with contact to prosthetic material is liable for biofilm or clot formation and TCHD malfunction. TCHD biofilms can create an altered micro-environment that facilitates slow-growing microorganisms where antibiotic penetration is difficult [9].

The decreased risk of CRBSI in ex-smokers is difficult to explain physiologically. Tobacco smoking cessation has been shown to augment the inflammation and immunity state in the patient, which may explain a reduction in CRBSI risk in our cohort [10].

Risk factors for CRBSI identified in previous studies include higher total intravenous iron dose, more frequent urokinase catheter infusion, local infection, and nasal carriage of *S. aureus* [5, 7, 11]. Data on these factors were incomplete at our center and were therefore not assessed in our study. In contrast to other studies, we found that duration of TCHD in situ and hypertension did not have a significant association with CRBSI. This may be due to our relatively low rate of CRBSI compared with the international literature [2, 3]. A median rate (IQR) of 0.59 (0.39–1.2) CRBSIs per 1000 catheter-days (tunneled and nontunneled HD catheters) was

reported in an Australian and New Zealand survey [12]. Our cohort of CRBSI episodes reflects primary TCHD insertions only. Other studies included serial TCHD insertions and repeat CRBSI episodes. Previous CRBSI is a risk factor for subsequent CRBSI [7]. In our study, fewer controls experienced a subsequent episode of CRBSI when compared with cases (4% vs 18%, respectively).

Almost half of the patients had a TCHD in situ for >90 days. This may reflect the 2 major reasons for TCHD insertion—acute start RRT or RRT access malfunction. Acute start RRT is due to late referrals and patients who do not engage in timely permanent access for RRT. Permanent vascular access takes weeks to months to fully mature and be ready for regular use. We also have a significant proportion of diabetic patients (42%), with underlying vascular disease or calcified vessels, which result in poor access development. Minimization of late referrals could be addressed with stronger community chronic kidney disease education, follow-up, and planning. Encouraging uptake of acute start peritoneal dialysis could reduce the need for vascular access. Our CRBSI microbiology results are consistent with the international literature. Most were gram-positive organisms, including *S. aureus* and coagulase-negative staphylococci. Gram-negative bacteremia and polymicrobial bacteremia have also been reported [3, 4].

This is the first Australian published data using multivariate analyses to identify intrinsic patient risk factors for CRBSI. Although the CRBSI rate is comparable to that reported in the international literature, more work is needed to achieve timely access for patients with near-end-stage kidney disease, including those with diabetes, and to avoid TCHD insertion into the left internal jugular vein.

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