

Haemodialysis vascular catheter-related blood stream infection: Organism types and clinical outcomes

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Abstract

Catheter-related bloodstream infection (CRBI) is an important complication of catheter use for haemodialysis, but it remains unclear whether clinical outcomes following CRBI are influenced by organism type. This study aims to compare clinical outcomes following CRBI from Gram-positive and non-Gram-positive organisms. This was a retrospective cohort study of patients with kidney failure receiving haemodialysis (HD) via vascular catheters who had a documented episode of CRBI in Western Australia between 2005 and 2018. The associations between organism type, likelihood of hospitalization, catheter removal and death from CRBI were examined using adjusted logistic regression models. There were 111 episodes of CRBI in 99 patients (6.1 episodes per 1000-catheter-days at risk). Of the study cohort, 53 (48%) were male and 38 (34%) identified as Aboriginal or Torres Strait Islander. Gram-positive organisms were identified in 73 (66%) CRBI episodes, most commonly *Staphylococcus aureus*. Of those with non-Gram-positive CRBI, 9 (24%) were attributed to *Pseudomonas aeruginosa*. One-hundred and two (92%) episodes of CRBI required hospitalization and 15 (13%) patients died from CRBI. Compared with non-Gram-positive CRBI, Gram-positive CRBI was associated with an increased risk of hospitalization and catheter removal, with adjusted odds ratio of 9.34 (95% CI 1.28–68.03) and 3.47 (95% CI 1.25–9.67), respectively. There was no association between organism type and death from CRBI. *Staphylococcus aureus* remains the most common organism causing CRBI in HD patients. CRBI is associated with substantial morbidity, particularly CRBI attributed to Gram-positive organisms.

KEYWORDS

bacteraemia, catheter complications, catheter related bloodstream infection, haemodialysis

1 | BACKGROUND

Catheter-related bloodstream infection (CRBI) is a frequent complication of vascular catheter use for haemodialysis (HD), with a reported incidence of 1.1–6.1 episodes per 1000 catheter days.¹ CRBI is

associated with substantial morbidity and mortality,² with a three-times greater risk of death compared to patients without bloodstream infection.³

Gram-positive organisms are responsible for almost 80% of all clinically relevant CRBI, with methicillin susceptible *Staphylococcus*

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aureus (MSSA) and methicillin resistant *Staphylococcus aureus* (MRSA) the most frequently isolated organisms.^{4,5} These organisms are associated with an excess risk of complicated hospitalisations, more often requiring intensive care unit (ICU) support compared to CRBI from Gram-negative organisms.⁶

We compared differences in the likelihood of catheter removal, hospitalization and death from CRBI between CRBI secondary to Gram-positive versus non-Gram-positive organisms in a cohort of HD patients in Western Australia (WA).

2 | METHODS

2.1 | Study population

This was a retrospective study of patients with kidney failure requiring HD treatment via tunnelled and non-tunnelled vascular catheters and had an episode of CRBI in WA between 2005 and 2018. The patients were identified by the Healthcare Infection Surveillance WA (HISWA), which collects data from the mandatory reporting of HD access-associated blood stream infections across all three tertiary hospitals in WA. This project was approved as a clinical audit by the respective hospital's human research ethics committee.

2.2 | Data collection

Data extracted from HISWA relating to the episode of CRBI included the vascular catheter type and organism(s). Baseline patient characteristics of age, sex, race, primary cause of kidney failure, presence of comorbid conditions at time of CRBI (diabetes and coronary artery disease) and duration of dialysis prior to CRBI; and infection-related characteristics including the prior history of MRSA, prior vascular catheter use, prior CRBI, date of catheter insertion, admission details [documented fever, white blood cell count (WCC) and C-reactive protein (CRP) level], and duration of hospitalization were extracted from local health-care records. Catheter antibiotic locks were typically used for all sites, but these data were not available.

2.3 | Exposure factor

CRBI was defined as positive blood culture (either catheter lumen or peripheral venous puncture) and clinical/laboratory suspicion of infection in the absence of other clinically evident infection source. Episodes of suspected CRBI in the absence of positive blood cultures were excluded. The primary exposure factor was the type of CRBI organism, categorized into infection from Gram-positive and non-Gram-positive organisms. For patients with CRBI from multiple organisms, they were included in the Gram-positive group if any Gram-positive organism was present. Organisms were

assessed for antibiotic resistance based on standard laboratory reporting of susceptibility available from local health-care records.

2.4 | Outcome measures

The primary outcomes were vascular catheter removal following the episode of CRBI and hospitalization directly attributed to CRBI. Secondary outcomes included ICU admission, metastatic infection and death from CRBI. Metastatic infection was defined as evidence of septic emboli from the primary source of infection. Death from CRBI was defined as death that occurred during the same admission as when the CRBI was identified by the clinical team.

2.5 | Statistical analysis

Data were expressed as number (percentages) for categorical variables and median (interquartile range) for non-normally distributed continuous variables, with comparisons between exposure groups undertaken using chi-square test and Kruskal-Wallis test, respectively. The associations between the exposure and outcome measures were examined using adjusted logistic regression analysis, with results expressed as adjusted odds ratio (OR) and 95% confidence interval (95% CI). Covariates included in the multi-variable models were selected a priori, and included age, sex, race, prior MRSA, prior vascular catheter use, prior CRBI and cause of kidney failure. Statistical analyses were performed using STATA statistical software IC version 15.1, with *p*-values of less than .05 considered statistically significant.

3 | RESULTS

3.1 | Study population

One hundred and eleven episodes of CRBI occurred in 99 patients (calculated as 6.1 episodes per 1000-catheter-days in patients who had experienced CRBI). Patient characteristics are shown in Table 1. The median (IQR) age of patients at time of CRBI was 57 (46–69) years, 53% were males and 38% identified as Aboriginal or Torres Strait Islander. Over 60% of patients in either group were maintained on dialysis for less than 12 months. One hundred and nine (98%) episodes of CRBI occurred in the presence of tunnelled catheters.

Gram-positive CRBI was identified in 73 (66%) episodes of CRBI, with MSSA and MRSA contributing 28 (38%) and 15 (21%) of Gram-positive isolates, respectively. The remaining Gram-positive isolates included coagulase negative staphylococci (predominantly *Staphylococcus epidermidis*) and *Enterococcus* species. Of the 38 episodes of non-Gram-positive CRBI, 9 (24%) and 7 (18%) were attributed to *Pseudomonas aeruginosa* and *Escherichia coli*, respectively. Thirteen (12%) episodes of CRBI were polymicrobial, and fungal CRBI was infrequent (*n* = 4 episodes).

TABLE 1 Baseline characteristics of the study cohort

	Total episodes of CRBI (n = 111)	Gram-positive CRBI (n = 73)	Non-Gram positive CRBI (n = 38)	p-Value
Patient demographics				
Age (median, IQR)	57 (46–69)	57 (44–67)	57 (46–70)	0.78
Male (n, %)	53 (47.7)	33 (45.2)	20 (52.6)	0.46
Aboriginal Torres-Strait Islander (n, %)	38 (34.2)	25 (34.2)	13 (34.2)	1.00
Cause of kidney failure (n, %)				
Diabetic nephropathy	66 (59.4)	46 (63)	20 (52.6)	0.29
Glomerulonephritis	18 (16.2)	9 (12.3)	9 (23.7)	
Other causes	27 (24.3)	18 (24.7)	9 (23.7)	
Comorbidities (n, %)				
Diabetes	71 (64)	49 (67.1)	22 (57.9)	0.34
Coronary artery disease	46 (41.4)	30 (41.1)	16 (42.1)	0.92
Haemodialysis duration (n, %)				
<1 year	69 (62.2)	46 (63.0)	23 (60.5)	0.22
1–5 years	25 (22.5)	20 (27.4)	5 (13.2)	
>5 years	17 (15.3)	7 (9.6)	10 (26.3)	
Infection details (n, %)				
MSSA	28 (25.2)	28 (38.4)	0 (0)	<.01
MRSA	15(13.5)	15 (20.5)	0 (0)	
<i>Pseudomonas aeruginosa</i>	9 (8.1)	0 (0)	9 (23.7)	
<i>Escherichia coli</i>	7 (6.3)	0 (0)	7 (18.4)	
Other	52 (46.8)	30 (41.1)	22 (57.9)	

Note: Data expressed as number (proportion) or as median and interquartile range (IQR).

Abbreviations: CRBI, catheter-related bloodstream infection; MRSA, methicillin-resistant *Staphylococcal aureus*; MSSA, methicillin-sensitive *Staphylococcal aureus*.

3.2 | Characteristics and outcomes according to types of CRBI

Table 2 compares the CRBI presentations and outcomes of patients with Gram-positive and non-Gram positive CRBI. A greater proportion of patients with Gram-positive CRBI required hospitalization (96% vs. 84%) and catheter removal (80% vs. 60%) compared to those with non-Gram-positive CRBI. Catheter removal rates for *Pseudomonas* CRBI (six of nine episodes, 66.7%) were similar to other non-Gram-positive CRBI. The median CRP and WCC levels were significantly higher in patients with Gram-positive CRBI compared to those without, and there was a shorter median time to catheter removal in patients with Gram-positive CRBI.

3.3 | Associations between CRBI types and clinical outcomes

Compared to patients with non-Gram-positive CRBI, patients with Gram-positive CRBI were more likely to require hospital admission and catheter removal, with adjusted OR of 9.34 (95% CI 1.28–68.03) and 3.47 (95% CI 1.25–9.67), respectively. There were no associations

between organism type and risks of ICU admission and death from CRBI (Table 3).

4 | DISCUSSION

In this contemporaneous cohort of HD patients with CRBI spanning 14 years, Gram-positive organisms were responsible for almost 70% of CRBI. Patients with Gram-positive CRBI were up to nine-times more likely to require catheter removal and hospitalization compared with non-Gram-positive CRBI, but the risks of mortality from CRBI and metastatic infection were similar. These findings suggest that Gram-positive organisms remain the dominant cause of CRBI and may be associated with a higher risk of morbidity compared to non-Gram-positive CRBI.

Previous studies have shown that Gram positive CRBIs were more likely to cause metastatic infection due to their propensity to form biofilms and adhere to native tissue.^{7,8} Consequently, there is likely to be systematic difference in the clinical management of CRBI conditional on the organism type. The perception by clinicians that MSSA and MRSA CRBIs are associated with poorer outcomes may encourage clinicians to adopt a more aggressive strategy of hospital admission, prescription of a longer course of intravenous antibiotics

TABLE 2 Laboratory and infection characteristics of the study cohort stratified by catheter-related bloodstream infection organism type

	Gram positive (n = 73)	Non-Gram positive (n = 38)	p-Values	MSSA (n = 28)	MRSA (n = 15)	Other Gram positive (n = 30)	p-Values ^a
Pre-catheter insertion (n, %)							
Prior catheters	30 (41.1)	21 (55.3)	0.155	10 (35.7)	4 (26.7)	16 (53.3)	0.144
Prior CRBI	16 (21.9)	10 (26.3)	0.604	5 (17.9)	1 (6.7)	10 (33.3)	0.199
Prior MRSA	20 (27.4)	7 (18.4)	0.296	4 (14.3)	8 (53.3)	8 (26.7)	0.027
Admission							
Fever (n, %)	53 (72.6)	29 (76.3)	0.031	19 (67.9)	13 (96.7)	21 (70.0)	0.073
WCC (x10 ⁹ /L)	12.9 (9.8–16.1)	9.8 (8.1–14.0)	0.039	12.8 (8.4–17.1)	15.6 (11.9–19.5)	11.3 (8.9–13.9)	0.054
CRP (ng/L)	125 (66–190)	69 (39–110)	0.007	125 (66–252)	171 (43–190)	120 (76–170)	0.022
Days from line insertion to CRBI (median, IQR)	58 (14–210)	72 (16–141)	0.837	36 (6–149)	47 (22–162)	117 (29–381)	0.260
Catheter removal (n, %)	58 (79.5%)	23 (60.5%)	0.030	24 (85.7)	15 (100.0)	19 (63.3)	0.007
Days from CRBI to catheter removal (median, IQR)	1 (1–3)	2 (1–2)	0.464	1 (1–2)	1 (1–2)	3 (1–4)	0.021
Hospitalization (n, %)	70 (95.9)	32 (84.2)	0.032	28 (100.0)	15 (100.0)	27 (90.0)	0.074
Days of hospitalization (median, IQR)	9 (6–16)	8 (6–14)	0.487	10 (7–19)	9 (7–25)	8 (5–13)	0.379
Admission to ICU (n, %)	10 (13.7)	2 (5.3)	0.174	4 (14.3)	2 (13.3)	4 (13.3)	0.993
Metastatic infection (n, %)	14 (19.2)	5 (13.2)	0.42	5 (17.9)	4 (26.7)	5 (16.7)	0.706
Death from CRBI (n, %)	11 (15.1)	4 (10.5)	0.507	7 (25.0)	0 (0.0)	4 (13.3)	0.122

Note: Data expressed as number (proportion) or as median and interquartile range (IQR).

Abbreviations: CRBI, catheter-related bloodstream infection; CRP, C-reactive protein; MRSA, methicillin-resistant *Staphylococcal aureus*; MSSA, methicillin-sensitive *Staphylococcal aureus*; WCC, white cell count.

^ap-Values denote comparisons between four groups of non-Gram positive, MSSA, MRSA and other Gram-positive organisms.

TABLE 3 Associations between catheter-related bloodstream infection organism type and clinical outcomes

	Catheter removal (OR, 95% CI)	Hospital admission (OR, 95% CI)	ICU admission (OR, 95% CI)	CRBI-related death (OR, 95% CI)
Gram-positive CRBI (vs. non-Gram-positive)	3.47 (1.25, 9.67)*	9.34 (1.28, 68.03)*	2.36 (0.42, 13.32)	1.43 (0.37, 5.49)
Polymicrobial	0.26 (0.06, 1.08)	0.13 (0.01, 1.73)	3.92 (0.65, 23.70)	0.56 (0.06, 5.41)
Age (per 10-years increase)	0.91 (0.61, 1.37)	1.41 (0.60, 3.27)	0.81 (0.52, 1.26)	1.41 (0.87, 2.28)
Male (vs. female)	1.65 (0.59, 4.59)	2.64 (0.36, 19.111)	0.61 (0.15, 2.47)	3.84 (1.02, 14.55)*
Prior MRSA	0.31 (0.10, 0.98)*	0.34 (0.05, 2.47)	1.15 (0.23, 5.89)	1.55 (0.38, 6.44)
Prior CRBI	0.64 (0.9, 2.20)	2.42 (0.25, 23.71)	-	0.94 (0.14, 6.43)
Prior catheters	0.43 (0.14, 1.32)	0.25 (0.03, 2.16)	0.80 (0.17, 3.71)	0.51 (0.12, 2.19)
Aboriginal Torres-Strait Islander	1.62 (0.46, 5.68)	1.87 (0.26, 13.38)	0.46 (0.08, 2.65)	1.82 (0.32, 10.21)
Diabetes	1.06 (0.37, 3.05)	0.11 (0.01, 1.52)	0.40 (0.09, 1.74)	1.20 (0.32, 4.52)

Note: Data expressed as adjusted odds ratio (OR) and 95% confidence interval (95% CI). Data expressed as adjusted odds ratio (OR) and 95% CI.

*Denotes $p < .05$.

Abbreviations: CRBI, catheter-related bloodstream infection; ICU, intensive care unit; MRSA, Methicillin-resistant *Staphylococcus aureus*.

(typically at least 14 days for uncomplicated *Staphylococcus aureus* bacteraemia⁹) and prompt removal of vascular catheters, which is reflected in our study showing a greater likelihood of hospital admission and a shorter median time to catheter removal in patients with Gram positive CRBI.¹⁰ Even though our study did not demonstrate a difference in the risk of metastatic infection and death from CRBI between organism types, it is noteworthy that almost 20% of CRBI required ICU admission, had evidence of metastatic infection or had

died from CRBI. These findings reinforce that CRBI continues to be associated with significant patient harm and excess health-care costs.

There are several limitations of note in this study. Cases of culture negative CRBI were not included in our study, which may have underestimated the true prevalence of CRBI. In addition, data of patients with catheters but without CRBI were not available and therefore, we were unable to calculate the CRBI rate for our population. Data relating to the use of prophylactic antibiotics pre-catheter insertion, type

and frequency of antibiotic catheter locks and the differences in the prescription or adherence to peri-catheter care (including the use of intranasal and topical mupirocin) were not available, all of which may have potentially modified our study findings.¹¹ There is likely to be treatment or centre bias as systematic differences in the management of CRBI are likely between clinicians and sites.

5 | CONCLUSION

This study has substantiated that CRBI from HD vascular catheters are associated with significant morbidity and mortality, particularly CRBI attributed to Gram-positive organisms. These findings support the need to identify patient-related characteristics and potentially modifiable catheter and procedural factors that contribute to the development of complicated CRBI.

AUTHOR CONTRIBUTIONS

Jessica Phillips was responsible for data collection. Jessica Phillips and Wai H. Lim were responsible for original drafting of the article. Wai H. Lim was responsible for the statistical analysis. Doris T. Chan, Aron Chakera, Ramyasuda Swaminathan, Khalil Patankar and Neil Boudville revised the article contents.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

This project was approved as a clinical audit project by the ethics committees of all three participating hospitals.

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