Hospitalization Risk and Long-term Complications Associated with Catheter-Related Bloodstream Infections Among Hemodialysis Patients

Krithika Rajagopalan[1], Kenneth Massey[2], Srini Rajagopalan[1], Stephen Imperiale-Hagerman[1], Paul Chew[2]

[1]Anlitiks Inc., [2]CorMedix Inc.

INTRODUCTION

- Patients on hemodialysis (HD) with central venous catheter (CVC) dependence (HD-CVC) are at high risk of developing catheter-related bloodstream infections (CRBSIs).[1,2]
- CRBSIs have an incidence of 2.5-5.5 cases per 1,000 catheter days, or 0.9-2.0 episodes per patient-year.[3]
- CRBSIs may result in life-threatening consequences such as stroke, myocardial infarction (MI), heart failure (HF), and endocarditis, and increased healthcare resource utilization (HCRU).[4,5,6]
- However, only a few studies have quantified the occurrence of these CRBSI-associated complications in the long-term and consequent HCRU trends.

OBJECTIVE

The aim of this study was to explore CRBSI-associated risk of long-term complications (LTCs) and HCRU among HD-CVC patients.

METHODS

Study Design and Data Source: Retrospective propensity score-matched case-control analysis using United States Renal Data System (USRDS), CROWNWeb (Consolidated Renal Operations in a Web-enabled Network), and Medicare claims spanning the period from 2013-2017.

Study Population:

The study population was selected in the following steps for assessment **(Figure 1)**:

- **Step 1**: All Medicare ESKD patients were identified during 2014-2016 and patients initiating CVC-dependent HD (HD-CVC) were selected.
- **Step 2:** Post CVC-insertion date, occurrence / no-occurrence of CRBSI (i.e., CRBSI /non-CRBSI) were identified on index date or assigned index date, respectively:
  - ***Index date - CRBSI group:*** First ICD-9/10-CM diagnostic claim for CRBSI (999.32/T80211x), catheter infection (999.31/ T80219x, T80218x) and sepsis/ bacteremia, or sepsis/bacteremia without occurrence of pneumonia, gangrene, or UTI within 3 days of hospitalization.
  - ***Assigned Index date - Non-CRBSI group:*** Date of CVC insertion + Reported Median days to CRBSI in the CRBSI group.
- Patients were excluded with one or more CVC or HD claims in the 6-months pre-index period or were diagnosed with sepsis/bacteremia who had pneumonia, gangrene or, urinary tract infection (UTI) greater than 3 days with hospitalization.
- **Step 3:** CRBSI/non-CRBSI patients were 1:1 propensity score-matched at CRBSI index/ assigned-index date on age, gender, race, comorbidities, Elixhauser comorbidity index, dialysis setting and diabetes medication.

Follow-up/Post-Index Period: Patients who survived until index date (CRBSI) or assigned index date (non-CRBSI) were followed for 1 year, loss to follow-up, or death.

Outcomes: Patient outcomes were assessed from index/assigned index date for 1 year:

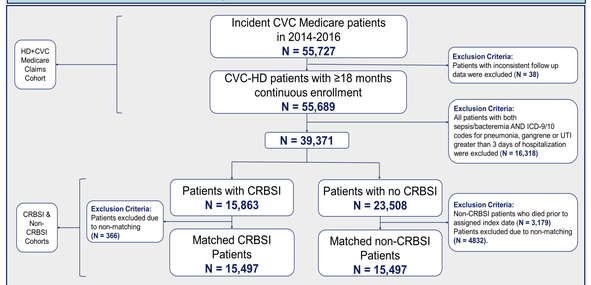
- Demographics: Age, gender, race, body mass index, comorbidities, Elixhauser Comorbidity Index.
- LTCs: Incidence and incremental rates of stroke, MI, HF, peripheral vascular disorder (PVD), dysrhythmia, endocarditis.
- HCRU measures: Total hospitalizations, length of stay (LOS), and outpatient visits.

Statistical Methods:

- Categorical and continuous variables were described using frequencies and percentages or means, medians, and standard deviations (SD), respectively.
- Incremental risk of LTCs were derived from differences in rates within CRBSI and non-CRBSI patients at 1 year.
- Differences between CRBSI and non-CRBSI patients with respect to baseline characteristics, HCRU, and LTCs were compared using non-parametric tests of Cramer's V and Wilcoxon tests, as appropriate.
- At 1 year post CRBSI, adjusted differences in HCRUs and time to LTCs were modeled using two-stage generalized linear models (GLM) with gamma log-link function and Cox proportional hazards models, respectively.

RESULTS

Figure 1. Patient Selection



CVC, central venous catheter; HD, hemodialysis; UTI, urinary tract infection; CRBSI, catheter-related bloodstream infection;

Table 1. Patient Demographics

Characteristics	CRBSI (n = 15,497)	Non-CRBSI (n = 15,497)	SMD	Cramer's V
Age	66.73	67.14	0.038	0.019
Gender (Female)	7,169 (46.3)	7,126 (46.0)	0.006	0.003
Race			0.035	0.017
African American	4,447 (28.7)	4,213 (27.2)		
Other / Unknown	677 (4.4)	664 (4.3)		
White	10,373 (66.9)	10,620 (68.5)		
Body Mass Index			0.030	0.015
Underweight	503 (3.3)	324 (2.8)		
Normal	4,247 (27.6)	3,179 (27.4)		
Overweight	3,973 (25.8)	2,982 (25.7)		
Obese	6,674 (43.3)	5,123 (44.1)		
Elixhauser Comorbidity Index			0.071	0.036
< 0	11,578 (74.7)	12,021 (77.6)		
0	26 (0.2)	27 (0.2)		
1 – 5	1,072 (6.9)	947 (6.1)		
6 – 13	2,421 (15.6)	2,194 (14.2)		
> 14	400 (2.6)	308 (2.0)		
Comorbidities				
CHF	8,469 (54.6)	8,204 (52.9)	0.034	0.017
COPD	1,981 (12.8)	1,832 (11.8)	0.029	0.015
CVA / TIA	1,683 (10.9)	1,575 (10.2)	0.023	0.011
Diabetes	8,926 (57.6)	8,865 (57.2)	0.008	0.004
GFR MDRD	12,805 (82.6)	13,121 (84.7)	0.055	0.028
Hypertension	5,063 (32.7)	4,982 (32.1)	0.011	0.006
Metastatic Cancer	290 (1.9)	242 (1.6)	0.024	0.012
Polycystic Disease	37 (0.2)	33 (0.2)	0.005	0.003
AIDS / HIV	181 (1.2)	125 (0.8)	0.037	0.018
Diabetes On Insulin	6,935 (44.8)	6,816 (44.0)	0.015	0.008
Diabetes On Oral Medications	1,725 (11.1)	1,751 (11.3)	0.005	0.003
Other Causes of ESKD	7,353 (47.4)	6,942 (44.8)	0.053	0.027
AVF Maturing			0.014	0.007
Yes	2,675 (17.3)	2,752 (17.8)		
No	12,033 (77.6)	11,944 (77.1)		
NA	789 (5.1)	801 (5.2)		
AVG Maturing			0.011	0.005
Yes	410 (2.6)	384 (2.5)		
No	14,049 (90.7)	14,064 (90.8)		
NA	1,038 (6.7)	1,049 (6.8)		

ESKD, end-stage kidney disease; BMI, body mass index; CHF, congestive heart failure; CVA/TIA, cerebrovascular accident/ transient ischemic attack; GFR MDRD, glomerular filtration rate at Stage 5 (i.e., ESKD) using modification of diet in renal disease equation; AIDS/ HIV, acquired immunodeficiency syndrome / human immunodeficiency virus; HD, hemodialysis, CAPD, continuous ambulatory peritoneal dialysis; AVF, arteriovenous fistula; AVG, arteriovenous graft, NA, not available.

RESULTS (Cont.)

- Patient demographics have been reported in **Table 1**.

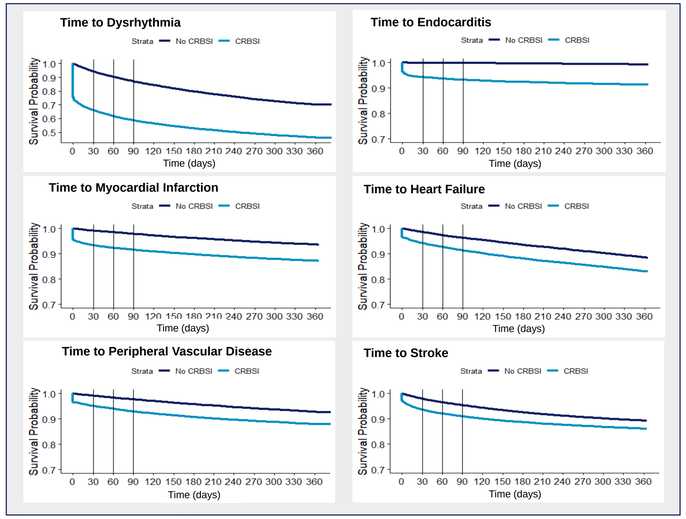
LTCs from Index/Assigned Index Date

- One-year incremental rates of LTCs in CRBSI patients vs. non-CRBSI patients ranged from 3.2% for stroke to 24.0% for dysrhythmia **(Table 2)**.
- As evidenced in the Kaplan-Meier survival curves, the disparity in cardiovascular complications between CRBSI and non-CRBSI patients in the year following index/assigned index dates was mostly accrued within 30 days of first occurrence of these events **(Figure 2)**.
- Adjusting for covariates, CRBSI resulted in significantly greater LTCs compared to non-CRBSI patients **(Table 3)**.

Table 2: Frequencies and Incremental risk of LTCs, at 1 year

Outcome	CRBSI (n = 15,497)	Non-CRBSI (n = 15,497)	Risk Difference	p-value	Cramer's V
Dysrhythmia	54.07%	30.05%	24.02%	< 0.001	0.155
Endocarditis	8.72%	0.73%	7.99%	<0.001	0.188
HF	17.03%	11.62%	5.41%	< 0.001	0.077
MI	12.80%	6.42%	6.38%	< 0.001	0.108
PVD	10.11%	6.45%	3.66%	< 0.001	0.065
Stroke	13.94%	10.74%	3.20%	< 0.001	0.049

Figure 2: Kaplan-Meier Survival Estimates of LTCs for CRBSI & Non-CRBSI Groups*



*Patients may have more than one LTC

Table 3. Association between CRBSI and LTCs, Cox Proportional Hazards Models*

	HR	95% CI	p-value
Dysrhythmia	2.45	2.33, 2.57	< 0.001
Endocarditis	12.4	9.97, 15.43	< 0.001
HF	1.52	1.42, 1.62	< 0.001
MI	2.11	1.94, 2.30	< 0.001
PVD	1.75	1.60, 1.91	< 0.001
Stroke	1.54	1.44, 1.65	< 0.001

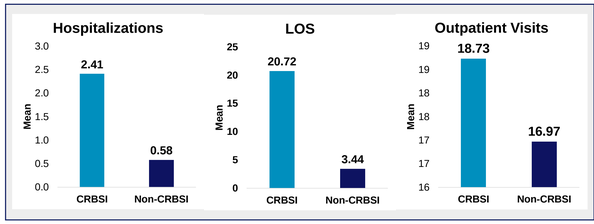
*Only covariates that were found to have a significant p-value < 0.05 were included in the model. Covariates included age, Elixhauser Comorbidity Index (ECI), race, BMI, gender, glomerular filtration rate at Stage 5 (i.e.,ESKD) modification of diet in renal disease (GFR MDRD), congestive heart failure (CHF), COPD, cerebrovascular accident / transient ischemic attack (CVA/TIA), diabetes, hypertension, metastatic cancer, and polycystic disease, other causes of ESRD, diabetic (on insulin), diabetic (on oral medication)

RESULTS (Cont.)

HCRU Measures (Figure 3)

- CRBSI patients had greater 1-year rates of hospital admissions (2.41 vs. 0.58, p < 0.001), length of stays (20.72 vs. 3.44 days, , p < 0.001) and outpatient visits (18.73 vs 16.97, , p < 0.001) compared to non-CRBSI patients.

Figure 3: Mean HCRU measures for CRBSI and non-CRBSI patients



Association of CRBSI and HCRU

- CRBSI was positively associated with hospital admissions (HR: 1.34, 95%CI: 1.29, 1.39) and LOS (HR: 2.13, 95%CI: 2.01, 2.27) compared to non-CRBSI patients (p-value <0.001).

LIMITATIONS

- The identification algorithm for CRBSI, which uses proxy determinates of disease, has the potential to misclassify the cause of bacteremia in patients.
- Due to insufficient information in this dataset, we were unable to determine whether patients had CVC still inserted at the time of bloodstream infections; however, the majority of bloodstream infections occurred within 6 months following CVC insertion.

CONCLUSIONS

- Following CRBSI there is increased risk of cardiovascular morbidity, including dysrhythmias, HF, MI, PVD, and stroke.
- Although all patients with HD-CVC are at high risk of endocarditis, those with CRBSI had more than ten-fold risk compared to non-CRBSI patients.
- As observed in the Kaplan-Meier curves, risk difference between LTCs mostly accrues within 30 days of index date.
- Compared to non-CRBSI patients, those with CRBSI had a four-fold rate in hospitalizations, with vastly greater duration of stay,
- Greater HCRU observed in CRBSI patients was due, in part, to increased risk of cardiovascular complications

REFERENCES

1. Gahlot R, Nigam C, Kumar V, Yadav G, Anupurba S. Catheter-related bloodstream infections. Int J Crit Illn Inj Sci. 2014;4(2):162-7.
2. Powe NR, Jaar B, Furth SL, Hermann J, Briggs W. Septicemia in dialysis patients: incidence, risk factors, and prognosis. Kidney Int. 1999;55(3):1081-90.
3. Allon M. Dialysis catheter-related bacteremia: treatment and prophylaxis. Am J Kidney Dis. 2004;44(5):779-91.
4. Ishani A, Collins AJ, Herzog CA, Foley RN. Septicemia, access and cardiovascular disease in dialysis patients: The USRDS Wave 2 Study1. Kidney Int. 2005;68(1):331-8.
5. Chaudry MS, Carlson N, Gislason GH, Kamper A-L, Rix M, Fowler VG, et al. Risk of Infective Endocarditis in Patients with End Stage Renal Disease. Clin J Am Soc Nephrol. 2017;12(11):1814.
6. Brunelli SM, Turenne W, Sibbel S, Hunt A, Pfaffle A. Clinical and economic burden of bloodstream infections in critical care patients with central venous catheters. J. Crit. Care. 2016;35:69-74.

QR CODE: PLACE HERE

Sponsored by CorMedix Inc.

ASN Kidney Week 2021, Nov. 4th – Nov. 7th, 2021, San Diego, CA