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MAJOR ARTICLE

Dialysis Catheter–related Bloodstream Infections in Patients Receiving Hemodialysis on an Emergency-only Basis: A Retrospective Cohort Analysis

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Background. An estimated 6500 undocumented immigrants with end-stage renal disease (ESRD) live in the United States. Those living in states that do not provide undocumented immigrants scheduled hemodialysis receive intermittent hemodialysis only when life-threatening conditions arise. Little is known about catheter-related bloodstream infections (CRBSIs) in this population.

Methods. We conducted a retrospective cohort study of emergency-only hemodialysis patients in the Harris Health System in Houston, Texas, between January 2012 and December 2015. We assessed CRBSI risk factors including demographics, comorbidities, and duration and frequency of hemodialysis. We investigated the microbiologic etiology of these infections, rates of recurrent CRBSI, and associated morbidity and mortality.

Results. The cohort included 329 patients; 90% were Hispanic, 60% had diabetes, and the average age was 51 years. A total of 101 CRBSIs occurred, with a rate of 0.84 infections per 1000 catheter-days. Cirrhosis and duration of hemodialysis during the study period were associated with increased risk of CRBSI. Seventeen CRBSIs were recurrent; infection with gram-positive bacteria predicted recurrence. Adherence to catheter-related infection guidelines was improved by infectious diseases consultation and associated with fewer recurrent infections. CRBSI was associated with prolonged hospitalization (mean, 15 days), composite complication rate of 8%, and a 4% mortality rate.

Conclusions. Patients receiving emergency-only hemodialysis via tunneled catheters have a high CRBSI rate compared with infection rates previously reported in patients receiving scheduled maintenance hemodialysis. Increased CRSBI risk likely contributes to the increased morbidity and mortality seen in ESRD patients receiving emergency-only hemodialysis.

Keywords. hemodialysis catheter; CRBSI; emergency hemodialysis; undocumented; ESRD.

More than 600 000 people with end-stage renal disease (ESRD) live in the United States [1]. While federal law provides US citizens with ESRD access to thrice-weekly scheduled hemodialysis, access to hemodialysis for America's estimated 6500 undocumented immigrants with ESRD varies by state [2]. The 1986 Consolidated Omnibus Budget Reconciliation Act prohibits federal Medicaid funds from financing nonemergency care for undocumented immigrants; however, the Emergency Medical Treatment and Labor Act allows use of Medicaid funds to treat undocumented immigrants for emergency medical conditions [3]. States have been largely left to decide for themselves what constitutes an emergency medical condition for undocumented immigrants with ESRD. This has produced national heterogeneity in the medical treatment of undocumented immigrants with ESRD, with states such as California and New York providing scheduled hemodialysis while other states provide emergency-only hemodialysis (hemodialysis offered only once a life-threatening condition—eg, severe hyperkalemia, acidosis, or respiratory distress—is present) [4].

In Texas, undocumented immigrants primarily receive emergency-only hemodialysis. The Harris Health System (HHS) in Houston, Texas, treats several hundred undocumented immigrants with ESRD [5]. The system's sole outpatient hemodialysis unit operates at capacity, providing scheduled maintenance hemodialysis for approximately 160 such patients. Several undocumented patients with ESRD have been able to purchase insurance off the exchange since the implementation of the Patient Protection and Affordable Care Act of 2014, which inhibits insurance agencies from excluding patients with any preexisting condition [6]. Unfortunately, despite HHS's limited capacity to provide standard maintenance hemodialysis to undocumented immigrants, and these patients' eligibility to purchase private insurance, HHS continues to treat several hundred undocumented patients with emergency-only hemodialysis.

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Compared with scheduled hemodialysis, emergency-only hemodialysis has been associated with greater use of emergency department and inpatient services, lower patient satisfaction, and higher costs [7]. Physicians who care for patients receiving emergency-only hemodialysis experience moral distress and emotional exhaustion from participating in what they perceive to be unjust care [8]. A recent study reported that patients receiving emergency-only hemodialysis have higher mortality and greater durations of hospitalization than patients who receive scheduled hemodialysis [9]. The study in question compared treatment outcomes among undocumented immigrants with ESRD who initiated standard or emergency-only hemodialysis at 1 of 3 large urban health centers between 2007 and 2014, finding that emergency-only hemodialysis was associated with a 14-fold higher 5-year mortality risk and an almost 10-fold higher rate of acute care usage. While this study observed similar rates of bacteremia between patients receiving emergency-only or scheduled hemodialysis (adjusted odds ratio, 2.31 [95% confidence interval, .80–6.70]; $P = .12$), the authors defined bacteremia without reference to clinical impression of infection to discriminate infection from culture contamination.

Permanent hemodialysis access with arteriovenous fistula or graft is infrequent among undocumented ESRD patients, especially among those receiving emergency-only hemodialysis [3, 5, 9]. Although hemodialysis catheters have been associated with higher morbidity and mortality than alternative forms of access in the scheduled hemodialysis population [1], whether hemodialysis catheters confer significant infection or mortality risk in undocumented ESRD patients has not been established. The present study characterizes the epidemiology and outcomes of hemodialysis catheter–related bloodstream infections (CRBSIs) in undocumented ESRD patients receiving emergency-only hemodialysis. We hypothesized that these patients would have a high prevalence of CRBSI associated with significant morbidity and mortality.

METHODS

Study Population

We conducted a retrospective analysis of patients who received emergency-only hemodialysis between 1 January 2012 and 31 December 2015 in the HHS in Houston, Texas. We identified patients using an electronic medical record dataset including all patients who undergo emergency-only hemodialysis at Ben Taub Hospital (BTH), the primary site for emergency-only hemodialysis in the HHS, maintained by the BTH inpatient hemodialysis unit. We included patients who received hemodialysis primarily through the BTH emergency department, excluding patients who received emergency-only hemodialysis in our system for <30 days or <5 times during the study period and those who were simultaneously receiving scheduled maintenance hemodialysis.

Definitions

For our study, we defined CRBSI using both blood culture and management criteria. Positive blood culture criteria consisted of recovery of the same microorganism from either 2 positive blood cultures from 2 different locations or 1 positive blood culture plus 1 positive catheter tip culture. Management criteria consisted of the treating physicians' identification of the infection as a probable CRBSI and the absence of an alternate suspected source of infection. This definition varies from the definition used in the Infectious Disease Society of America (IDSA) guidelines and was chosen recognizing the limited availability of cultures from hemodialysis catheter ports in our data. In BTH, hemodialysis catheter cultures may only be obtained by hemodialysis nurses, and medical teams did not delay antibiotic therapy awaiting nurse availability for cultures. We defined CRBSI as recurrent when the patient had a prior CRBSI involving the same microorganism during the study; in each case, negative blood cultures were obtained between episodes.

Duration of emergency hemodialysis was calculated as the period from the later of either 1 January 2012 or the date of hemodialysis initiation to the earlier of the date of last hemodialysis therapy or 31 December 2015. Periods during which the patient did not have emergency hemodialysis in our system for >30 days were not included to account for the possibility that the patient may have received hemodialysis outside HHS, which reflected our preference to overestimate rather than underestimate the CRBSI rate in our cohort. Frequency of hemodialysis was calculated by dividing the total number of hemodialysis sessions by the duration of hemodialysis in months. Hemodialysis sessions during admissions for CRBSI were not included in this calculation.

Predictors and Outcomes

We collected data on demographics (age, sex, and ethnicity), comorbidities (diabetes mellitus, cirrhosis, and human immunodeficiency virus), type of hemodialysis access, duration and frequency of emergency-only hemodialysis, and number of incident and recurrent CRBSIs with microbiologic etiologies and outcomes. For each CRBSI we recorded the duration of hospitalization as well as complications including intensive care unit (ICU) stays, osteomyelitis, endocarditis, septic arthritis, septic emboli, and death. To evaluate predictors of recurrent infection, we recorded the prescribed antibiotic regimen and duration, whether and how the infected catheter was replaced, how definitive antibiotic therapy was administered, and whether the treatment plan adhered to the recommendations of the IDSA's clinical practice guidelines for the diagnosis and management of intravascular catheter–related infections [10]. Specifically, we examined 3 parameters of conformity to the guidelines: whether the patient received guideline-recommended antibiotics, whether the patient was prescribed the recommended

duration of therapy, and whether the infected catheter was managed appropriately. For pathogens not mentioned in the guideline, we considered antibiotic selection appropriate if the patient received an antibiotic with activity against the organism, duration appropriate if the patient received at least 2 weeks of antibiotics, and catheter management appropriate if the catheter was removed.

Statistical Analysis

Patients were stratified into 2 groups based on whether they had any CRBSI. We compared the distribution of demographic characteristics, comorbidities, and duration and frequency of hemodialysis between the 2 groups. Categorical variables were described as proportions and compared using the χ^2 test. Continuous variables were described as means and standard deviations and compared using Student *t* test.

Among patients with CRBSI, we used logistic regression to compare the risk of catheter exchange between primary and recurrent CRBSIs and used linear regression to compare the duration of antibiotic treatment between these groups. The correlation of CRBSIs of the same patient was adjusted using generalized estimating equation. We used negative binomial regression to assess the association between microbiology of the infection for the primary infection and occurrence of recurrent infection. A significance value of .05 was used to determine statistically significant differences for all analyses.

RESULTS

Four hundred and eighty-seven patients met the initial inclusion criteria for evaluation and 158 patients were excluded based on criteria mentioned earlier. Table 1 displays patient characteristics of the 329 individuals analyzed in our cohort, stratified by the occurrence of at least 1 CRBSI during the study period. Patients in the study cohort had an average age of 51 years, 90% were Hispanic, and 60% had diabetes mellitus; the subset of patients who developed CRBSI was demographically similar. We found no statistically significant differences in comorbidities between the 2 groups, but observed a trend toward a greater prevalence of cirrhosis among patients with CRBSI (13.8% vs 6.4%; $P = .052$). Patients with CRBSI had a longer duration of hemodialysis (15.5 ± 9.7 months vs 11.6 ± 8.5 months; $P = .002$) but no difference in frequency of hemodialysis (5.3 ± 1.9 sessions/month vs 5.4 ± 2.2 sessions/month; $P = .46$). Of the 249 patients who stopped emergency-only hemodialysis before the end of the study period, 37% were lost to follow-up, 20% obtained scheduled hemodialysis outside HHS, 15% died, 14% obtained scheduled hemodialysis at HHS's outpatient hemodialysis center, 8% left Houston, 4% entered hospice care, and 2% stopped for other reasons (eg, recovering renal function, initiating peritoneal dialysis).

Sixty-five of our 329 patients had at least 1 CRBSI and 16 patients had multiple CRBSIs. A total of 101 CRBSIs occurred over a total of 120 138 catheter-days within the cohort, yielding a CRBSI rate of 0.84 per 1000 catheter-days. Seventeen CRBSIs met our criteria for recurrent infection. The mean interval between CRBSI recurrence was 120 days. Infection with gram-positive bacteria predicted recurrence (relative risk [RR], 2.18; $P < .0001$), which was driven primarily by infection due to *Staphylococcus aureus* (RR = 2.66; $P < .0001$).

The microbiology of CRBSIs in our cohort is described in Table 2. Sixty-five CRBSIs involved gram-positive bacteria, 35 involved gram-negative bacteria, and 1 involved a nontuberculous mycobacterium. Polymicrobial infection occurred in 9 cases. CRBSI due to methicillin-sensitive *S. aureus* (MSSA) and

Table 1. Emergency-only Hemodialysis Patient Characteristics Stratified by Catheter-related Bloodstream Infection Occurrence

Characteristic	Patients With CRBSIs (n = 65)	Patients Without CRBSIs (n = 264)	*P* Value
Age, y (SD)	52.4 ± 12.2	51.2 ± 14.9	.45
Male sex	34 (52.3)	147 (55.7)	.31
Ethnicity			
Hispanic	58 (89.2)	240 (90.9)	.35
African American	3 (4.6)	14 (5.3)	.41
Middle Eastern	2 (3.1)	4 (1.5)	.25
Asian	2 (3.1)	6 (2.3)	.36
Diabetes mellitus	43 (66.2)	153 (58.0)	.11
Cirrhosis	9 (13.8)	17 (6.4)	.052
HIV	1 (1.3)	1 (0.4)	.23
Duration of hemodialysis, mo (SD)	15.5 ± 9.7	11.6 ± 8.5	.002[a]
Frequency of hemodialysis, sessions/mo (SD)	5.3 ± 1.9	5.4 ± 2.2	.46

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: CRBSI, catheter-related bloodstream infection; HIV, human immunodeficiency virus; SD, standard deviations.

[a]Statistically significant.

Table 2. Emergency-only Hemodialysis Catheter–related Bloodstream Infection Microbiology

Organism	No. of Isolates (n = 101)
Gram-positive bacteria	65 (64.4)
Methicillin-sensitive *Staphylococcus aureus*	25 (24.8)
Methicillin-resistant *Staphylococcus aureus*	17 (16.8)
Coagulase-negative staphylococci	14 (13.9)
Enterococcus faecalis	5 (5.0)
Other	4 (4.0)
Gram-negative bacteria	35 (34.7)
Enterobacter spp	17 (16.8)
Klebsiella spp	4 (4.0)
Pseudomonas spp	2 (2.0)
Stenotrophomonas spp	2 (2.0)
Escherichia coli	1 (1.0)
Others	9 (8.9)
Mycobacterium chelonae subsp *abscessus*	1 (1.0)

Data are presented as No. (%).

methicillin-resistant *S. aureus* occurred at relative rates comparable to our hospital's antibiogram (data not shown).

Associations between the rate of recurrent infection and the infected catheter's management, the method of delivering definitive antimicrobial therapy, and adherence to treatment guidelines are shown in Table 3. We found no difference in the rate of recurrent infection between patients receiving catheter exchange over guidewire vs removal and later replacement (10% vs 16.4%; $P = .6$); this was also true for the subset of CRBSI due to *S. aureus* (33% vs 29%; $P = .87$). Catheter salvage was not associated with more recurrent infections than exchange or removal (22% vs 16%, $P = .5$); however, when catheter salvage was attempted in CRBSI due to *S. aureus*, recurrence occurred in 50% of cases. Nineteen percent of patients were planned to complete parenteral antibiotics dosed after hemodialysis on a scheduled basis via our emergency-only hemodialysis system; in these cases, physicians documented the treatment plan in the electronic medical record and provided the patient a letter indicating the treatment plan. Nonetheless, patients treated with posthemodialysis dosing via our emergency-only hemodialysis system missed 1 or more antibiotic doses in 47% of cases and trended toward a higher rate of recurrent infections vs patients receiving any other treatment modality (32% vs 14%; $P = .06$).

Nonadherence to treatment guidelines mostly involved CRBSIs due to *S. aureus*. All but 1 case of inappropriate antibiotic selection involved CRBSI due to MSSA treated with an agent other than nafcillin, oxacillin, or cefazolin; the majority received vancomycin, but 1 patient each received ceftriaxone, clindamycin, levofloxacin, or ciprofloxacin. All cases of inappropriate duration of therapy involved *S. aureus* infections for which a prolonged antibiotic course was indicated. Indications for favoring prolonged therapy primarily involved incomplete workup for complications (eg, lack of venous ultrasound to evaluate for septic thrombophlebitis, lack of echocardiography or receipt of transthoracic but not transesophageal echocardiography, failure to document negative blood cultures at 72 hours); however, 2-week therapy was pursued despite attempted catheter salvage in 6 cases, positive blood cultures at 72 hours in 2 cases, and septic thrombophlebitis in 1 case. Every case of inappropriate catheter management involved catheter salvage in patients with *S. aureus* CRBSI.

Recurrent CRBSI was more common among patients prescribed an inappropriate duration of therapy (36% vs 9%; $P = .001$) or who had inappropriate catheter management (50% vs 15%; $P = .025$); appropriate antibiotic selection was not associated with recurrence (18% vs 7%; $P = .25$). Infectious diseases consultation, obtained in 30% of cases, was associated with higher rates of appropriate antibiotic selection (100% vs 80%; $P = .006$), prescribed antibiotic duration (87% vs 62%; $P = .01$), catheter management (100% vs 92%; $P = .13$), and adherence to all 3 aspects of care (87% vs 58%; $P = .005$), but not lower rates of recurrent infection (16.9% vs 16.7%; $P = .98$) or in-hospital mortality (0% vs 4%; $P = .35$).

Hospitalizations for CRBSI lasted a mean of 15 days and 18% involved an ICU stay, lasting a mean of 2 days. Composite CRBSI complication rate was 8% and included osteomyelitis (1/101), infective endocarditis (3/101), septic arthritis (2/101), and septic emboli (2/101). Four patients died of CRBSI, yielding a 4% per-episode mortality rate. Thirty-eight subjects (12% of the cohort) died during the study period. Cardiovascular events accounted for 12 deaths, and the consequences of emergency-only hemodialysis (ie, hyperkalemia and metabolic

Table 3. Management of Catheter-related Bloodstream Infection and Subsequent Recurrent Infection

Management	Recurrent Infection (n = 17)	No Recurrent Infection (n = 85)
Management of the infected catheter		
Removal and later replacement[a]	12 (71)	61 (72)
Direct exchange over guidewire	1 (6)	9 (11)
Retained (line salvage)	4 (24)	14 (16)
Administration of definitive antibiotic therapy		
Completed full course as inpatient	8 (47)	36 (42)
Outpatient oral antibiotics	2 (12)	28 (33)
Via OPAT with PICC	0 (0)	2 (2)
Via temporary outpatient scheduled hemodialysis	1 (6)	4 (5)
Via "scheduled" hemodialysis using the emergency-only hemodialysis system[a]	6 (35)	13 (15)
Adherence to IDSA guidelines for management of intravascular catheter–related infections		
Appropriate antibiotic selection	16 (94)	71 (84)
Inappropriate antibiotic selection	1 (6)	13 (15)
Appropriate duration of therapy	6 (35)	64 (75)
Inappropriate duration of therapy	11 (65)	20 (24)
Appropriate catheter management	14 (82)	81 (95)
Inappropriate catheter management	3 (18)	3 (4)

Abbreviations: IDSA, Infectious Diseases Society of America; OPAT, outpatient parenteral antibioitic therapy; PICC, peripherally inserted central catheter.

[a]New catheters were placed a median of 5 days later (range, 1–18 days); in those with longer durations, temporary hemodialysis catheters were placed as needed.

acidosis) contributed in 50% of cases. Infections other than CRBSI accounted for 8 deaths and included pneumonia, intraabdominal and soft tissue infection, and sepsis of undetermined origin. Intracranial hemorrhage accounted for 2 deaths and gastrointestinal hemorrhage for 1 death; cause of death was unknown in the remaining cases.

DISCUSSION

In this retrospective analysis of emergency-only hemodialysis patients within the HHS between 2012 and 2015, we observed a CRBSI rate of 0.84 infections per 1000 catheter-days. Patients with CRBSI received longer durations of emergency-only hemodialysis. Seventeen percent of CRBSIs were recurrent; infection with gram-positive bacteria, and particularly *S. aureus*, was a risk factor for recurrent infection. Adherence to catheter-related infection guidelines was improved by infectious diseases consultation and associated with fewer recurrent infections. Delivering scheduled posthemodialysis doses of antibiotics via the emergency hemodialysis system was an unreliable treatment modality. CRSBI was associated with hospitalizations averaging 15 days, a complication rate of 8%, and 4% mortality.

Table 4 summarizes hemodialysis CRBSI rates previously reported in the United States. Rates of CRBSI may be decreasing due to the Fistula First Campaign resulting in decreased hemodialysis catheter use and the "Scrub the Hub Protocol" initiated by the Centers for Disease Control and Prevention to decrease CRBSI incidence [1, 11]. A recent assessment of outpatient scheduled hemodialysis units reported a CRBSI rate of only 0.59 infections per 1000 catheter-days [12]. The only other study evaluating CRBSI rates in patients receiving emergency-only hemodialysis reported a CRBSI rate of 2.61 infections per 1000 catheter-days [13]. These findings suggest that patients who receive emergency-only hemodialysis have more CRBSIs than their contemporaries receiving scheduled hemodialysis.

This study has certain limitations. First, it was retrospective and conducted within a single hospital system. Second, our patients rely predominantly on tunneled hemodialysis catheters for hemodialysis access, whereas hemodialysis catheter use is less common in scheduled hemodialysis patients; this limits our ability to make direct comparisons between these groups. Third, we may have underestimated the true rate of CRBSI-attributable bloodstream infection in the cohort, as in our experience through-catheter blood cultures are not always obtained prior to antibiotic administration. Fourth, our patients may have received care outside the HHS for CRBSIs, leading us to underestimate the CRBSI rate, though our study attempted to correct for this by excluding periods >30 days during which the patient did not receive hemodialysis within the HHS from the catheter-days calculation.

There are multiple means to address the high CRBSI rate in patients receiving emergency-only hemodialysis. One straightforward solution is to provide scheduled hemodialysis to all patients with ESRD, which has already been accomplished in multiple states [2, 9]. Shen and colleagues recently reported that renal transplantation outcomes in nonresident aliens were equivalent to better than those in US citizens, suggesting that transplantation would also be an effective means of treating ESRD in undocumented patients [20]. While not addressing the other inequities associated with emergency-only hemodialysis, the elevated CRBSI risk could be mitigated by transitioning patients from catheters to arteriovenous fistulas or grafts for hemodialysis access, as these are associated with lower rates of bloodstream infection [21], or with antimicrobial lock therapy, which prevents catheter infections in patients receiving scheduled hemodialysis [22].

In conclusion, our emergency-only hemodialysis patients experienced a higher rate of CRBSI than reported in recent studies of patients receiving scheduled hemodialysis. These CRBSIs were accompanied by prolonged hospitalizations, complicated by serious invasive infections, and resulted in several deaths. CRBSIs add to the burdens of emergency-only hemodialysis: diminished quality and quantity of life for undocumented patients with

Table 4. Comparison of Incident Catheter-related Bloodstream Infection Reported in Literature

Study Author, Year [Reference]	No. of CRBSIs	Catheter-Days	Incident Rate, per 1000 Catheter-Days
Saad, 1999 [14]	86	15 636[a]	5.5
Stevenson et al, 2002 [15]	123	53 947[a]	2.28[b]
Maki et al, 2006 [16]	596	372 500[a]	1.6
Camins et al, 2010 (control group) [17]	37	17 126[a]	2.16[b]
Al-Solaiman et al, 2011 [18]	184	58 044[a]	3.17
Hymes et al, 2017 (control group) [12]	107	177 337	0.59
Rojas-Moreno et al, 2016 [13]	134	51 341[a]	2.61
Present study	101	120 138	0.84

Abbreviation: CRBSI, catheter-related bloodstream infection.

[a]The catheter-days were calculated based on the number of CRBSI and incident rate. For example, in [13], catheter days = 1000 × 134 / 2.61.

[b]Rate was reported as 5.2 bloodstream infections (BSIs) per 1000 hemodialysis sessions in control period in [17]. In a similar study by Taylor et al, hemodialysis sessions averaged 1 per 2.41 patient days (28.81 per 10 000 hemodialysis procedures / 11.97 per 10 000 patient-days) [19]. Thus, we converted 5.2 BSIs per 1000 hemodialysis sessions to 2.16 (ie, 5.2 / 2.41) BSIs/patient-days.

ESRD, moral distress for the healthcare professionals who care for them, and increased costs for hospitals and society.

Notes

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