American Journal of Infection Control 47 (2019) 381–386

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major Article

Role of transfusions in the development of hospital-acquired urinary tract–related bloodstream infection among United States Veterans

M. Todd Greene PhD, MPH [a,b,*], Sanjay Saint MD, MPH [a,b], David Ratz MS [a], Latoya Kuhn MPH [a], Jennifer Davis MHSA [a], Payal K. Patel MD, MPH [a,b], Mary A.M. Rogers PhD [b]

[a] *Veterans Affairs Ann Arbor Healthcare System, Ann Arbor, MI*
[b] *Department of Internal Medicine, University of Michigan, Ann Arbor, MI*

Key Words:
Healthcare–associated infection
Blood transfusion

Background: Urinary tract–related bloodstream infection (BSI) is associated with substantial morbidity, mortality, and financial costs. We examined the role of red blood cell (RBC) transfusions on developing this condition among US Veterans.

Methods: We conducted a matched case-control study among adult inpatients admitted to 4 Veterans Affairs hospitals. Cases were patients with a positive urine culture result obtained 48 hours or longer after admission and a blood culture obtained within 14 days of the urine culture, which grew the same organism. Controls included patients with a positive urine culture result who were at risk for but did not develop BSI (control group 1) and patients without a positive urine culture result who were present in the facility at the time of case diagnosis (control group 2).

Results: Compared with the findings in control group 1, receipt of RBCs was not significantly associated with urinary tract–related BSI (odds ratio, 1.03; 95% confidence interval, 1.00-1.07; $P = .07$). However, we found increased odds of urinary tract–related BSI compared with the results in patients without infection (control group 2) (odds ratio, 1.11; 95% confidence interval, 1.06-1.17; $P < .001$).

Conclusions: Given the heightened risk of urinary tract–related BSI associated with receiving a greater number of RBC transfusions, adhering to recommendations to transfuse the minimum amount of blood products necessary may minimize the risk of this infection among Veterans.

Knowing the contributors to bloodstream infection (BSI) is a crucial precursor to developing patient safety practices for prevention. The urinary tract is considered a contributor to dissemination of microorganisms to the bloodstream; the percentage of patients with bacteriuria who subsequently develop bacteremia is estimated at 3%.[1] The incidence of nursing home–acquired BSI was reported at a similar rate of 0.3 per 1,000 resident-days, but when BSI occurs, the urinary tract accounts for 50% of such episodes.[2] In acute care hospitals, 21% of BSIs are reported to be secondary to a urinary source.[3] This is important because treating patients with BSIs is challenging, and mortality rates among patients with urinary tract–related BSIs have been estimated between 13% and 30%.[4,5]

Previously identified risk factors for urinary tract–related BSI include age,[6,7] male sex,[7-9] urinary tract disease,[6,10] urinary tract procedure,[9] chronic kidney disease,[11] malignancy,[7] neutropenia,[10] elevated serum creatinine,[12] low serum albumin,[12] diabetes mellitus,[7,12] liver disease,[10] dementia,[11] cigarette use,[7] indwelling urethral catheters,[6,9,13] immunosuppressant therapy,[7,9,10] and red blood cell (RBC) transfusion.[14]

Because blood transfusion practices among hospitalized patients have changed considerably over the past 20 years,[15] and male sex has consistently been found to confer increased risk of developing urinary tract–related BSI,[16] we were particularly interested in examining the role of RBC transfusions on developing this disease among predominantly male US Veterans. In addition, although numerous risk factors for urinary tract–related BSI have been identified previously, published findings have been derived from single-site studies. We therefore conducted a multisite, matched case-control study on adult

* Address correspondence to M. Todd Greene, PhD, MPH, 2800 Plymouth Rd, NCRC Bldg 16, Rm 470C, Ann Arbor, MI 48109.
E-mail address: mtgreene@med.umich.edu (M.T. Greene).

Funding/support: This project was supported by a Veterans Affairs Clinical Sciences Research & Development Merit Review Award (EPID-011-11S). The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the US government.
Conflicts of interest: None to report.

https://doi.org/10.1016/j.ajic.2018.09.013
0196-6553/

veterans hospitalized at 4 Veterans Affairs (VA) hospitals to examine factors that may alter the risk of urinary tract–related BSI.

METHODS

Setting

Patients were identified at 4 diverse VA Medical Centers (1 in the South and 3 in the Midwest) between January 1, 2000, and December 31, 2014. The VA Ann Arbor Healthcare System's institutional review board approved this study.

Case Definition

Nosocomial urinary tract–related BSI in adult patients (aged ≥ 18 years) were defined as follows: (1) a positive urine culture and blood culture with the same organism during their hospital stay; (2) the urine culture must have been obtained 48 hours or longer after admission; (3) the blood culture must have been obtained on the same day or after the urine culture, but within 14 days of the urine culture; and (4) the urine culture must show growth of at least 10^3 colony-forming units (CFU)/mL of the single organism. Manual record review was performed for all cases to identify and exclude cases that displayed evidence of primary BSI with hematogenous spread to the kidney (eg, central line–associated BSI, endocarditis). We had 2 registered nurses separately perform chart abstraction of the cases to identify and exclude cases of primary BSI. A physician with experience in infectious disease–related studies reviewed a random sample of cases and also adjudicated any discordant views between the registered nurses.

Control Selection

All controls were selected using incidence density sampling. Controls were matched to each case by calendar time (within 90 days) when the BSI occurred in the case, by sex, and by hospital. A 1:4 ratio of cases to controls was used for matching whenever possible.

Control Group 1

Control group 1 included all adult patients with a positive urine culture (as defined earlier) who were at risk for but did not develop a BSI during their hospital stay (ie, negative blood culture or no blood culture ordered). The explicit goal for this control group was to determine factors that influenced the spread of a microorganism in the urinary tract to the bloodstream. The exposure period for these controls was similar to that of the matched cases; in other words, if the BSI occurred 10 days after the UTI in the case, then the matched control exposure period would likewise be the 10-day period after the UTI.

Control Group 2

The risk set for control group 2 included all adult patients without a positive urine culture (as defined earlier) who were present in the facility at the time of case diagnosis. These were patients who had a negative urine culture result or did not have a urine culture ordered. Because a substantial number of patients may well have had a positive urine culture result even in the absence of symptomatic, clinical UTI, this second control group was included to avoid the control requirement of a urinalysis. The exposure period was the time from admission to BSI for the respective matched case.

Data Collection

Demographic, clinical, microbiological, and blood bank data were extracted from the VA electronic medical record. All urine and blood cultures were ordered and collected at the clinical discretion of healthcare providers, and conventional microbiological methods were used for identification of microorganisms from cultures. Comorbid conditions were defined using Elixhauser comorbidity coding with ICD-9-CM codes.

Statistical Analysis

Preliminary analyses included an assessment of mean ± SD for continuous variables and percentage for categorical variables. Differences in the frequency of identified microorganisms (*genus)* between cases and controls (control group 1) were assessed using the χ^2 test. To account for the matched design, conditional logistic regression was used to assess adjusted associations between the cases and each control group separately. The full model contained the following explanatory variables: age, race, surgical procedures (cardiovascular, digestive, and urologic), cancer, diabetes mellitus, renal failure, liver disease, and medications (antibacterial, statins, and immunosuppressants), as well as units of RBCs, platelets, and plasma received. We used $\alpha = 0.05$ (2 tailed) for all statistical tests. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Of the 569 patients who met the case definition, 67 were deemed to be "seeding" cases after medical chart review, 2 had a previous BSI with the same organism before admission, and 1 had no urine CFU, with the data leaving 499 eligible cases for analysis. Urine and blood culture collections were done on the same day in most cases (66%), 1 day apart in 10%, and 2 or more days apart in 24%. The median time between admission and BSI was 12 days.

Descriptive characteristics for all 3 groups are presented in Table 1. For control group 1, 482 cases (97.0%) achieved our goal of a 1:4 case-control ratio (1,959 total matches). Among the cases, 65.8% had urine culture values ≥ 10^5 CFU/mL (ie, more stringent than our 10^3 CFU/mL inclusion criteria), whereas 57.8% of the controls reached the same threshold. Cases were more likely to have renal failure ($P = .002$) and malignancy ($P = .02$), to undergo cardiovascular ($P < .001$) and digestive system ($P < .001$) procedures, and to receive RBC products ($P < .001$). Cases also spent more days in the intensive care unit ($P = .004$) and were more likely to die during hospitalization ($P < .001$). For control group 2, 488 cases (98.4%) achieved the 1:4 matching ratio (1,967 total matches). Compared with control group 2, cases were older ($P < .001$) and more likely to have renal failure ($P < .001$) and cancer ($P = .001$); to undergo cardiovascular ($P < .001$), digestive system ($P < .001$), and urologic procedures ($P < .001$); and to receive RBC products ($P < .001$). Cases were also more likely to spend more time in the intensive care unit ($P < .001$), to have a longer length of stay ($P < .001$), and to die during hospitalization ($P < .001$).

Microorganism percentages for cases and controls are presented in Table 2. The most common microorganisms were *Enterococcus* spp (18.1%), *Staphylococcus* spp (17.5%), *Candida* spp (16.7%), and *Escherichia coli* (14.6%). Cases were more likely to be infected with *Staphylococcus* spp ($P < .001$). The breakdown of *Staphylococcus* spp identified among cases (n = 182) was as follows: *Staphylococcus epidermidis*, 67 (36.8%); coagulase-negative *Staphylococcus* (species unknown), 58 (31.9%); and *Staphylococcus aureus* 57 (31.3%). Among the 57 *S aureus* organisms identified among cases, 15 (26.3%) were methicillin resistant and 3 (5.3%) were methicillin sensitive.

Multivariable conditional logistic regression results comparing cases with both control groups are shown in Table 3. After adjusting

Table 1
Descriptive characteristics of cases and controls

Characteristic	Cases (n = 499)	Control group 1 (n = 1959)	Control group 2 (n = 1967)	*P* value*	*P* value†
Demographic data					
Male sex, n (%)	492 (98.6)	1,939 (99.0)	1,940 (98.6)	.47	.96
Age, y, mean ± SD	67.2 (12.3)	67.1 (12.1)	61.8 (13.3)	.95	<.001
Race, n (%)					
White	281 (56.3)	1,126 (57.5)	1,210 (61.5)	.76	.10
Black	175 (35.1)	654 (33.4)	600 (30.5)	—	—
Other	43 (8.6)	179 (9.1)	157 (8.0)	—	—
Length of stay, d, mean ± SD	46.8 (89.0)	39.3 (50.2)	25.0 (29.5)	.07	<.001
BMI, mean ± SD‡	26.2 (6.9)	26.3 (7.2)	27.4 (6.6)	.72	.001
ICU days before BSI, mean ± SD	12.2 (63.8)	3.9 (8.9)	1.8 (5.3)	.004	<.001
Died during hospitalization, n (%)	121 (24.2)	159 (8.1)	55 (2.8)	<.001	<.001
Comorbidities, n (%)					
Diabetes	137 (27.4)	542 (27.7)	535 (27.2)	.92	.91
Renal failure	93 (18.6)	259 (13.2)	189 (9.6)	.002	<.001
Liver disease	43 (8.6)	141 (7.2)	133 (6.8)	.28	.15
Malignancy	50 (10.0)	134 (6.8)	117 (5.9)	.02	.001
Procedures, n (%)					
Cardiovascular	195 (39.1)	452 (23.1)	360 (18.3)	<.001	<.001
Digestive	130 (26.1)	344 (17.6)	247 (12.6)	<.001	<.001
Urologic	34 (6.8)	72 (3.7)	39 (2.0)	.002	<.001
Medications§					
Antibiotics	149 (29.9)	693 (35.4)	476 (24.2)	.02	.009
Immunosuppressants	72 (14.4)	207 (10.6)	144 (7.3)	.02	<.001
Statins	142 (28.5)	593 (30.3)	503 (25.6)	.43	.19
Receipt of blood products, n (%)					
RBCs	194 (38.9)	581 (29.7)	376 (19.1)	<.001	<.001
Platelets	38 (7.6)	83 (4.2)	64 (3.3)	.002	<.001
Plasma	61 (12.2)	156 (8.0)	115 (5.8)	.003	<.001

P values are derived using the χ^2 (categorical variables) or *t* test (continuous variables). Control group 1 included all adult patients with a positive urine culture result who were at risk for but did not develop a BSI during their hospital stay (ie, negative blood culture result or no blood culture ordered). Control group 2 included all adult patients without a positive urine culture result (ie, negative urine culture result or no urine culture ordered) who were present in the facility at the time of case diagnosis.
BMI, body mass index; *BSI*, bloodstream infection; *ICU*, intensive care unit; *RBCs*, red blood cells.
*Cases versus control group 1.
†Cases versus control group 2.
‡BMI data missing for 31 cases, 132 controls from control group 1, and 232 controls from control group 2.
§Medication received 2 days before the date of BSI.

for age, race, comorbidities, surgical procedures, medications received, and other blood products received the number of RBC transfusions was not significantly associated with increased odds of urinary tract–related BSI when comparing cases with control group 1 (adjusted odds ratio [aOR], 1.03; 95% confidence interval [CI], 1.00-1.07; *P* = .07) and significantly associated with increased odds of urinary tract–related BSI when comparing cases with control group 2 (aOR, 1.11; 95% CI, 1.06-1.17; *P* < .001).

Because transfusions are within the hypothesized causal pathway between surgery (via blood loss) and BSI, in a secondary analysis we excluded all surgical procedures from our multivariable models. Compared with both control groups, cases receiving RBC transfusions had significantly increased odds of developing urinary tract–related BSI (aOR, 1.05, 95% CI, 1.02-1.09, *P* = .002, and aOR, 1.17, 95% CI, 1.12-1.23, *P* < .001 relative to control groups 1 and 2, respectively).

DISCUSSION

Several important findings have emerged from our study. First, *Staphylococcus* spp and *E coli* were the most common pathogens identified in our cohort of US Veterans with urinary tract–related BSI.[17] Second, some of our findings confirm previously identified risk factors for the development of urinary tract–related BSI.

Table 2
Distribution of microorganisms among cases and control group 1

Microorganism	Cases (n = 499)	Control group 1 (n = 1959)	Total (n = 2,458)	*P* value
Staphylococcus spp	182 (36.5)	249 (12.7)	431 (17.5)	<.001
Escherichia coli	96 (19.2)	262 (13.4)	358 (14.6)	.001
Candida spp	51 (10.2)	359 (18.3)	410 (16.7)	<.001
Pseudomonas spp	45 (9.0)	172 (8.8)	217 (8.8)	.87
Klebsiella spp	42 (8.4)	144 (7.4)	186 (7.6)	.42
Enterococcus spp	29 (5.8)	416 (21.2)	445 (18.1)	<.001
Proteus spp	18 (3.6)	91 (4.6)	109 (4.4)	.31
Enterobacter spp	15 (3.0)	43 (2.2)	58 (2.4)	.29
Other*	21 (4.2)	223 (11.4)	244 (9.9)	<.001

Control group 1 included all adult patients with a positive urine culture result (as defined earlier) who were at risk for but did not develop a BSI during their hospital stay (ie, negative blood culture result or no blood culture ordered).
**Acinetobacter* spp, *Alcaligenes* spp, *Streptococcus* spp, *Bacillus* spp, *Burkholderia cepacia*, *Citrobacter* spp, *Corynebacterium* spp, *Diptheroids* spp, *Gardnerella vaginalis*, *Hafnia alvei*, *Lactobacillus* spp, *Morganella morganii*, *Providencia* spp, *Legionella pneumophilia*, and *Serratia* spp.

Table 3
Predictors of hospital-acquired urinary tract–related BSI

Characteristic	Cases versus control group 1 OR (95% CI)	*P* value	Cases versus control group 2 OR (95% CI)	*P* value
Age	1.00 (0.99-1.01)	.60	1.03 (1.02-1.04)	<.001
Race				
White (reference)	Reference	—	Reference	—
Black	1.06 (0.84-1.34)	.62	1.29 (1.01-1.65)	.04
Other/unreported	1.02 (0.70-1.50)	.91	1.25 (0.84-1.88)	.27
Surgical procedures				
Cardiovascular	1.99 (1.58-2.50)	<.001	2.26 (1.75-2.92)	<.001
Digestive	1.54 (1.19-1.99)	0.001	1.90 (1.43-2.51)	<.001
Urologic	1.79 (1.15-2.79)	0.01	3.27 (1.93-5.54)	<.001
Comorbidities				
Diabetes mellitus	0.99 (0.78-1.25)	0.90	0.96 (0.75-1.23)	.72
Renal failure	1.39 (1.04-1.86)	0.03	1.48 (1.08-2.05)	.02
Liver disease	1.17 (0.80-1.72)	0.43	1.62 (1.08-2.44)	.02
Malignancy	1.42 (1.00-2.04)	0.05	1.44 (0.97-2.12)	.07
Medications received*				
Antibiotics	0.68 (0.53-0.86)	0.001	0.99 (0.77-1.27)	.95
Immunosuppressants	1.38 (1.02-1.89)	0.04	2.15 (1.52-3.04)	<.001
Statin	1.00 (0.79-1.28)	0.98	1.13 (0.87-1.47)	.37
Blood products†				
RBCs	1.03 (1.00-1.07)	0.07	1.11 (1.06-1.17)	<.001
Platelets	0.98 (0.86-1.12)	0.77	0.93 (0.81-1.07)	.29
Plasma	1.00 (0.95-1.05)	0.89	0.98 (0.92-1.05)	.55

Control group 1 included all adult patients with a positive urine culture result who were at risk for but did not develop a BSI during their hospital stay (ie, negative blood culture result or no blood culture ordered). Control group 2 included all adult patients without a positive urine culture result (ie, negative urine culture result or no urine culture ordered) who were present in the facility at the time of case diagnosis.
BSI, bloodstream infection; *CI*, confidence interval; *OR*, odds ratio; *RBCs*, red blood cells.
*Medications modeled as being administered during the hospital stay 2 days before the index date (ie, the BSI date of the case) within each matched case-control set.
†Number of transfusions.

Third, RBC transfusions during hospitalization were associated with urinary tract–related BSI.

Previous studies have identified Enterobacteriaceae,[7] *Enterococcus* spp,[5,10] a*nd E coli*[6] as the most commonly isolated microorganisms in patients with urinary tract–related BSI. In the present study, *Enterococcus* spp were the most common microorganisms isolated in urine cultures; however, similar to a previous study of urinary tract–related BSI among Veterans,[7] here *Enterococcus* spp were more common in controls than in cases. Conversely, *Staphylococcus* spp, the second most common microorganisms in the present study, were more frequently isolated in the cases. Saint et al[7] also found that *Staphylococcus* spp, although less frequently isolated overall, were more frequently isolated in veterans with urinary tract–related BSIs. Taken together, these findings suggest a potentially unique role of *Staphylococcus* spp in the development of urinary tract–related BSIs among veterans specifically. This has important implications for veterans' care, given that complicated urinary tract infection caused by *Staphylococcus* spp is often caused by antibiotic-resistant strains and is strongly associated with urinary catheterization.[18] Furthermore, catheter-associated urinary tract infection caused by methicillin-resistant *S aureus* disseminates to bacteremia more frequently and rapidly compared with infections caused by other bacteria.[18-20] In the present study, 64.9% of cases had an indwelling urinary catheter at some point between hospital admission and the date of urinary tract–related BSI. Furthermore, previous studies have shown higher urinary catheter use in VA settings compared with non-VA settings.[21,22]

Our study both confirms and extends previous work on the identification of risk factors for urinary tract–related BSI. A recent systematic review found that male sex, neutropenia, malignancy, liver disease, receipt of immunosuppressant medications, and RBC transfusions were the most consistently identified risk factors conferring an increased risk of developing urinary tract–related BSIs.[16] In our study of predominantly male US Veterans with urinary tract–related BSIs, compared with control group 1, our findings confirm the previously identified associations between malignancy and receipt of immunosuppressant medications. In addition, we detected an association between renal failure and increased risk of urinary tract–related BSI, an association detected in a previous study.[10] Urologic procedures are also a known risk factor for urinary tract–related BSI.[9,10] Our findings support the previously detected associations between urologic procedures and also suggest that patients undergoing other surgical procedures (specifically cardiovascular and digestive) may be at increased risk of developing urinary tract–related BSIs. The statistically significant associations between cases and control group 1 were also detected between cases and control group 2, helping rule out the possibility that identified associations were confounded by urinalysis orders.

There was a dose response in the odds of urinary tract–related BSI when compared with patients without infection (ie, control group 2); for each unit of RBCs, the odds of BSI increased by 11%. The primary mechanism by which this occurs may be immunomodulation,[23] which was first recognized in the 1970s when transfusions were used as immunosuppressants. Since then, RBC transfusions have been associated with the incidence of BSI in hospitalized patients,[24,25] particularly in surgical patients. In our study, RBC transfusions appear to be within the causal pathway between surgery and urinary tract–related BSI. A larger prospective study is needed to separate the effects of transfusion from those of surgery and the procedures associated with the surgery. In addition, we found that in nonsurgical patients, the odds of urinary tract–related BSIs were increased after RBC transfusions. Similarly, a previous study indicated that patients receiving RBC transfusions had nearly 5-fold greater odds of developing urinary tract–related BSIs compared with those not receiving transfusions.[14] However, in that study, most patients were women. RBC transfusions tend to be more common in women because the threshold for administration is not sex specific, and women normally have lower hemoglobin levels than men. In our present study, nearly all the patients were male, and the use of blood products was closely associated with surgical procedures (rather than

iron deficiency anemia). For the surgical patients, we could not completely distinguish whether the increased risk of BSI was owing to the surgical procedures or the blood products; however, for the nonsurgical patients, RBC transfusion was clearly associated with BSI.

Another mechanism for the association between transfusion and infection is through the introduction of microorganisms, although this is less likely to occur. In healthy individuals, blood transiently contains microorganisms[26,27]; however, in the United States, donated blood is tested for human immunodeficiency virus, hepatitis B and C, human T-lymphotropic virus, and syphilis, with periodic testing for West Nile virus and Chagas disease in certain areas. There are ongoing improvements in pathogen-reducing treatments for blood products.[28] Unfortunately, additional data regarding the specific blood products were not available in this dataset. More recent evidence indicates that characteristics of blood donors, including age and sex, may affect the response of the recipients.[29,30]

Despite underlying gender differences, our study provides additional support for the connection between receipt of RBC transfusion and healthcare–associated infection generally. As such, judicious use of blood transfusions may help enhance patient safety. A meta-analysis of randomized controlled trials has shown that restrictive transfusion strategies are associated with reduced risk of healthcare–associated infections (particularly for serious infections) compared with liberal transfusions strategies.[31] Recent updates to clinical practice guidelines from the AABB (formerly the American Association of Blood Banks) indicate that restrictive strategies in which the transfusion is not indicated until the hemoglobin level is 7 g/dL are safe in most hemodynamically stable hospitalized adult patients.[32] These guideline updates are in concert with the American Society of Hematology's recommendation for the Choosing Wisely initiative to only transfuse the minimum amount of RBC units necessary.[33] In line with these recommendations, blood transfusions have decreased among US Veterans between 2000 and 2010.[34]

Our study has several limitations. First, it might not always be clear whether a positive urinary culture result in a patient with bacteremia represents urinary tract–related BSI or hematogenous seeding of a primary BSI or bacteremia from an alternate source, particularly in cases with positive culture results with microorganisms not traditionally viewed as primary uropathogens. The retrospective nature of our study affected our ability to determine whether positive urine culture results reflected a primary urinary infectious nidus or seeding from a hematogenous site. We addressed this by conducting manual chart reviews and excluding cases felt to have a clear competing BSI source. Second, we did not confirm that isolates from the urine and blood were identical organisms using antimicrobial resistance patterns or molecular typing methods. Third, although this was a multisite study performed in 4 VA hospitals, the generalizability of our findings to all Veterans may be limited. Fourth, considering that the characteristics of blood donors vary, each unit of blood is slightly different in composition. Furthermore, there may be differences in preservatives and storage duration for the blood products, which we could not discern in this study.

CONCLUSIONS

Limitations notwithstanding, our multicenter case-control study of US veterans has findings relevant to hospital infection prevention policy and clinical practice. We found that certain patients—those with malignancy, renal failure, undergoing surgical procedures, or receiving immunosuppressant medications—are at greater risk for developing BSIs, and thus efforts to reduce modifiable risk factors (eg, implementing strategies to reduce urinary catheters[35]) are warranted. In addition, patients with a suspected urinary tract source of BSI may warrant empiric antibacterial coverage of common pathogens, such as *Staphylococcus* spp. Finally, endeavoring to transfuse the minimum amount of blood products necessary in a hospitalized patient remains a prudent approach.

Acknowledgments

We thank Debbie Zawol, MSN, RN, ACNS-BC, Karen Schumacher, RN, and Derek Dimcheff, MD, PhD for their roles in reviewing medical records of cases to rule out cases that displayed evidence of primary bloodstream infections with hematogenous spread to the kidney.

References

1. Saint S. Clinical and economic consequences of nosocomial catheter-related bacteriuria. Am J Infect Control 2000;28:68-75.
2. Mylotte JM. Nursing home-acquired bloodstream infection. Infect Control Hosp Epidemiol 2005;26:833-7.
3. Fortin E, Rocher I, Frenette C, Tremblay C, Quach C. Healthcare-associated bloodstream infections secondary to a urinary focus: the Quebec provincial surveillance results. Infect Control Hosp Epidemiol 2012;33:456-62.
4. Bryan CS, Reynolds KL. Hospital-acquired bacteremic urinary tract infection: epidemiology and outcome. J Urol 1984;132:494-8.
5. Chang R, Greene MT, Chenoweth CE, Kuhn L, Shuman E, Rogers MA, et al. Epidemiology of hospital-acquired urinary tract-related bloodstream infection at a university hospital. Infect Control Hosp Epidemiol 2011;32:1127-9.
6. Jerkeman M, Braconier JH. Bacteremic and non-bacteremic febrile urinary tract infection: a review of 168 hospital-treated patients. Infection 1992;20:143-5.
7. Saint S, Kaufman SR, Rogers MA, Baker PD, Boyko EJ, Lipsky BA. Risk factors for nosocomial urinary tract-related bacteremia: a case-control study. Am J Infect Control 2006;34:401-7.
8. Krieger JN, Kaiser DL, Wenzel RP. Urinary tract etiology of bloodstream infections in hospitalized patients. J Infect Dis 1983;148:57-62.
9. Conway LJ, Liu J, Harris AD, Larson EL. Risk factors for bacteremia in patients with urinary catheter-associated bacteriuria. Am J Crit Care 2016;26:43-52.
10. Greene MT, Chang R, Kuhn L, Rogers MA, Chenoweth CE, Shuman E, et al. Predictors of hospital-acquired urinary tract-related bloodstream infection. Infect Control Hosp Epidemiol 2012;33:1001-7.
11. Bursle EC, Dyer J, Looke DF, McDougall DA, Paterson DL, Playford EG. Risk factors for urinary catheter associated bloodstream infection. J Infect 2015;70:585-91.
12. Leibovici L, Greenshtain S, Cohen O, Wysenbeek AJ. Toward improved empiric management of moderate to severe urinary tract infections. Arch Intern Med 1992;152:2481-6.
13. Bahagon Y, Raveh D, Schlesinger Y, Rudensky B, Yinnon AM. Prevalence and predictive features of bacteremic urinary tract infection in emergency department patients. Eur J Clin Microbiol Infect Dis 2007;26:349-52.
14. Rogers MA, Blumberg N, Heal JM, Kuhn L, Greene MT, Shuman E, et al. Role of transfusion in the development of urinary tract-related bloodstream infection. Arch Intern Med 2011;171:1587-9.
15. Goodnough LT, Maggio P, Hadhazy E, Shieh L, Hernandez-Boussard T, Khari P, et al. Restrictive blood transfusion practices are associated with improved patient outcomes. Transfusion 2014;54:2753-9.
16. Conway LJ, Carter EJ, Larson EL. Risk factors for nosocomial bacteremia secondary to urinary catheter-associated bacteriuria: a systematic review. Urol Nurs 2015;35:191-203.
17. Patel PK, Greene MT, Rogers MAM, Ratz D, Kuhn L, Davis J, et al. The epidemiology of hospital-acquired urinary tract-related bloodstream infection in veterans. Am J Infect Control 2018;46:747-50.
18. Walker JN, Flores-Mireles AL, Pinkner CL, Schreiber IV HL, Joens MS, Park AM, et al. Catheterization alters bladder ecology to potentiate *Staphylococcus aureus* infection of the urinary tract. Proc Natl Acad Sci U S A 2017;114:E8721-30.
19. Al Mohajer M, Musher DM, Minard CG, Darouiche RO. Clinical significance of *Staphylococcus aureus* bacteriuria at a tertiary care hospital. Scand J Infect Dis 2013;45:688-95.
20. Muder RR, Brennen C, Rihs JD, Wagener MM, Obman A, Stout JE, et al. Isolation of *Staphylococcus aureus* from the urinary tract: association of isolation with symptomatic urinary tract infection and subsequent staphylococcal bacteremia. Clin Infect Dis 2006;42:46-50.
21. Mody L, Greene MT, Meddings J, Krein SL, McNamara SE, Trautner BW, et al. A national implementation project to prevent catheter-associated urinary tract infection in nursing home residents. JAMA Intern Med 2017;177:1154-62.
22. Tsan L, Langberg R, Davis C, Phillips Y, Pierce J, Hojlo C, et al. Nursing home-associated infections in Department of Veterans Affairs community living centers. Am J Infect Control 2010;38:461-6.
23. Vamvakas EC, Blajchman MA. Transfusion-related immunomodulation (TRIM): an update. Blood Rev 2007;21:327-48.

24. Banbury MK, Brizzio ME, Rajeswaran J, Lytle BW, Blackstone EH. Transfusion increases the risk of postoperative infection after cardiovascular surgery. J Am Coll Surg 2006;202:131-8.
25. Shorr AF, Jackson WL, Kelly KM, Fu M, Kollef MH. Transfusion practice and blood stream infections in critically ill patients. Chest 2005;127:1722-8.
26. Gosiewski T, Ludwig-Galezowska AH, Huminska K, Sroka-Oleksiak A, Radkowski P, Salamon D, et al. Comprehensive detection and identification of bacterial DNA in the blood of patients with sepsis and healthy volunteers using next-generation sequencing method—the observation of DNAemia. Eur J Clin Microbiol Infect Dis 2017;36:329-36.
27. Nikkari S, McLaughlin IJ, Bi W, Dodge DE, Relman DA. Does blood of healthy subjects contain bacterial ribosomal DNA? J Clin Microbiol 2001;39:1956-9.
28. Salunkhe V, van der Meer PF, de Korte D, Seghatchian J, Gutiérrez L. Development of blood transfusion product pathogen reduction treatments: a review of methods, current applications and demands. Transfus Apher Sci 2015;52:19-34.
29. Chassé M, McIntyre L, English SW, Tinmouth A, Knoll G, Wolfe D, et al. Effect of blood donor characteristics on transfusion outcomes: a systematic review and meta-analysis. Transfus Med Rev 2016;30:69-80.
30. Chassé M, Tinmouth A, English SW, Acker JP, Wilson K, Knoll G, et al. Association of blood donor age and sex with recipient survival after red blood cell transfusion. JAMA Intern Med 2016;176:1307-14.
31. Rohde JM, Dimcheff DE, Blumberg N, Saint S, Langa KM, Kuhn L, et al. Health care-associated infection after red blood cell transfusion: a systematic review and meta-analysis. JAMA 2014;311:1317-26.
32. Carson JL, Guyatt G, Heddle NM, Grossman BJ, Cohn CS, Fung MK, et al. Clinical practice guidelines from the AABB: red blood cell transfusion thresholds and storage. JAMA 2016;316:2025-35.
33. American Society of Hematology. Choosing wisely: ten things physicians and patients should question. Available from: http://www.choosingwisely.org/wp-content/uploads/2015/02/ASH-Choosing-Wisely-List.pdf. Accessed November 5, 2018.
34. Rogers MAM, Greene MT, Burns JD, Ratz D, Kuhn LE, Saint S, et al. A longitudinal study of transfusion utilization in hospitalized veterans. J Clin Outcomes Manag 2017;24: 404-11.
35. Saint S, Greene MT, Krein SL, Rogers MA, Ratz D, Fowler KE, et al. A program to prevent catheter-associated urinary tract infection in acute care. N Engl J Med 2016;374:2111-9.