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ABSTRACT

INTRODUCTION: Critically ill patients and their pharmacokinetics present complexities often not considered by consensus guidelines from the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Prior surveys have suggested discordance between certain guideline recommendations and reported infectious disease pharmacist practice. Vancomycin dosing practices, including institutional considerations, have not previously been well described in the critically ill patient population.

OBJECTIVES: To evaluate critical care pharmacists' self-reported vancomycin practices in comparison to the 2009 guideline recommendations and other best practices identified by the study investigators.

METHODS: An online survey developed by the Research and Scholarship Committee of the Clinical Pharmacy and Pharmacology (CPP) Section of the Society of Critical Care Medicine (SCCM) was sent to pharmacist members of the SCCM CPP Section practicing in adult intensive care units in the spring of 2017. This survey queried pharmacists' self-reported practices regarding vancomycin dosing and monitoring in critically ill adults.

RESULTS: Three-hundred and sixty-four responses were received for an estimated response rate of 26%. Critical care pharmacists self-reported largely following the 2009 vancomycin dosing and monitoring guidelines. The largest deviations in guideline recommendation compliance involve consistent use of a loading dose, dosing weight in obese patients, and quality improvement efforts related to systematically monitoring vancomycin-associated nephrotoxicity. Variation exists regarding pharmacist protocols and other practices of vancomycin use in critically ill patients.

CONCLUSION: Among critical care pharmacists, reported vancomycin practices are largely consistent with the 2009 guideline recommendations. Variations in vancomycin dosing and monitoring protocols are identified, and rationale for guideline non-adherence with loading doses elucidated.

KEYWORDS: Vancomycin, critical care, therapeutic drug monitoring, guideline, continuous infusion, dose, monitoring

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Introduction

From 2009-2020, guidelines for vancomycin dosing were available through a joint effort from the American Society of Health-System Pharmacists (ASHP), the Infectious Diseases Society of America (IDSA), and the Society of Infectious Diseases Pharmacists (SIDP).[1] Despite availability of these guidelines and over 50 years of clinical experience, much remains unknown regarding the optimal use of vancomycin in clinical practice.[2] A 2013 survey of infectious diseases pharmacists revealed discordance between vancomycin practices and guideline recommendations, particularly regarding a reluctance to use loading doses in seriously ill patients, to use actual body

†SCCM-CPP is reserved for the final author position as this work is a collective work from the section

weight for dose calculation in obesity, and to systematically monitor for complications such as nephrotoxicity.[3]

The compliance of pharmacists and physicians with guideline recommendations for vancomycin dosing and monitoring is important from an overall antimicrobial stewardship perspective, but is of particular importance in the critical care setting for several reasons. The complexities of the intensive care unit (ICU) patient population introduce additional challenges to a complex drug. The acuity of the patient population demands adequate pharmacokinetic-pharmacodynamic target attainment for serious, life-threatening infections while minimizing the risk of nephrotoxicity for patients already at risk of acute kidney injury and often simultaneously prescribed multiple other nephrotoxins. Critically ill patients' clearance of vancomycin could vary, from significant decreases in acute kidney injury to clinically significant increases in the setting of augmented renal clearance. Adjustments for other medical therapies, such as continuous renal replacement therapy (CRRT) and other dialysis modalities, represent unique circumstances that may not be addressed by guidelines. Other "best practice" items related to vancomycin dosing in the critically ill are likely variable across ICU pharmacists due to unique aspects of this patient population.

If any discordant areas of practice deviate in a substantial way from guideline recommendations, understanding factors driving critical care pharmacists' decisions to do so are important to elucidate and represent cornerstones of implementation science efforts. The purpose of this survey was to determine if this variability exists in an effort to potentially inform future guideline recommendations and to reduce variability in evidence-based practices. We sought to build on a prior survey of vancomycin use[3] in the following ways: (1) To perform a more recent survey of practice patterns given the continuously updated literature on vancomycin since 2013, (2) To study under which clinical scenarios ICU pharmacists may not adhere to guideline recommendations and ascertain why, (3) To characterize practice patterns regarding ICU-centric dosing challenges that may not be addressed in consensus guidelines, and (4) To explore respondent characteristics associated with compliance to guideline recommendations or early adoption of certain vancomycin dosing practices.

Materials and methods

Survey design

A survey was developed by a pharmacist working group of the Society of Critical Care Medicine (SCCM) Clinical Pharmacy and Pharmacology (CPP) Research and Scholarship Committee in early 2017. This survey was approved by the University of Kentucky Institutional Review Board as an exempt study.

Survey questions were developed by the working group using the 2009 ASHP/IDSA/SIDP guidelines as a template.[1] Once guideline recommendations were addressed in the survey, additional survey questions were created to capture areas of what the authors considered "best practice" or areas where substantial variability in practice was hypothesized to exist; for example, whether pharmacists were alerted to initiation or discontinuation of renal replacement therapies to adjust dosing accordingly. The survey was a 24-item questionnaire, with six general demographic questions, eight vancomycin-related demographic questions regarding the practice site, and 10 questions related to individual clinician's vancomycin dosing practices (Appendix).

A modified Likert scale was used: rarely (<10% of the time); sometimes (10-50% of the time); often (51-90% of the time); and routinely (>90% of the time) was used for questions of which a frequency of a particular action was inquired (eg. how often a clinician would recommend an intervention). A pilot survey was performed by five non-critical care pharmacists to establish face and content validity of the survey instrument. Six critical care pharmacists not involved on the study team took the survey to estimate time required for completion and provide any additional feedback or areas for clarification. Verbal and written feedback from all pilot tests were incorporated into the final survey by the research team. The survey required approximately 10-15 minutes for completion.

Cross-sectional survey

Invitations to complete the survey were sent over e-mail twice, two weeks apart during April of 2017. The survey was administered through and data collected using REDCap electronic data capture tools hosted at the University of Kentucky.[4] Invitations were sent out electronically via SCCM staff to all SCCM members of the CPP section, which includes pharmacist and non-pharmacist members. Pharmacist members of CPP practicing in adult critical care settings were specifically invited to take the survey and represent the target population of interest. Non-pharmacist members, or pharmacists practicing in a pediatric critical care setting, were asked not to respond to the survey.

Statistical analysis

Data were analyzed with Stata (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). Categorical data from the survey are presented as proportions. Exploratory logistic regression analyses were undertaken to evaluate factors associated with the following: selection of often or routinely (eg. >50% of the time) for loading doses for all six clinical scenarios examined, use of area-under-the-curve (AUC) as pharmacokinetic target parameter, and self-reported comfort with AUC calculations (ie. somewhat or extremely comfortable). Candidate predictor variables identified *a priori* by the study team thought to influence vancomycin dosing practices included: region, practitioner years of experience, hospital type, hospital size, and ICU type. Due to complete separation of variables in some of the regression models, a penalized maximum likelihood regression model was used with the *firthlogit* package in Stata.[5-7] Output from regression models are presented as odds ratios (OR) with 95% confidence intervals (CI). Two-sided *P*-value <.05 was considered statistically significant.

Table 1. Respondent demographics.

	NUMBER (%)
Practice Region	
Midwestern United States	111/364 (30.5)
Southern United States	109/364 (30.0)
Western United States	74/364 (20.3)
Northeastern United States	60/364 (16.5)
Outside of United States	10/364 (2.7)
Institutional Setting	
Academic medical center/urban	174/364 (47.8)
Community hospital/teaching/urban	89/364 (24.5)
Community hospital/non-teaching/urban	44/364 (12.1)
Other (including government and rural hospitals)	57/364 (15.6)
Institution Size	
<250 beds	55/364 (15.1)
250-499 beds	119/364 (32.7)
500-750 beds	99/364 (27.2)
>750 beds	91/364 (25.0)
Current Level of Training	
Current PGY2 specialty pharmacy resident (any specialty)	35/364 (9.6)
Practitioner less than 5 years out from terminal training	121/364 (33.2)
Practitioner 5-10 years out from terminal training	104/364 (28.6)
Practitioner more than 10 years out from terminal training	99/364 (27.2)
Other	5/364 (1.4)
Primary Location or Service	
Cardiothoracic ICU	20/364 (5.5)
Emergency Department	20/364 (5.5)
Medical ICU	109/364 (29.9)
Mixed Medical/Surgical ICU	115/364 (31.6)
Surgical/Trauma ICU	49/364 (13.5)
Other	51/364 (14.0)
Pharmacists Physically Round with the Primary or Intensivist Team ⩾5 days/Week	
Yes	332/364 (91.2)

Results

Survey response rate

The survey was delivered to 2,305 SCCM CPP members (includes pharmacists and non-pharmacists) via e-mail using the SCCM CPP section distribution list. Approximately 1,500 of these members are pharmacists within the CPP section per the SCCM demographic database. Based on internal demographic data from the section indicating that approximately 100 pharmacists practiced in pediatric critical care, we estimate that 1,400 of these pharmacists practiced in an adult ICU setting and would be eligible for the survey. We received 364 responses, for an estimated response rate of 26%.

Respondent demographics

Respondent demographics are presented in Table 1. Approximately half (48%) of respondents were from urban academic medical centers. The two most frequent responses for institutional bed size were 250-499 beds and 500-750 beds. The large majority of respondents (>97%) were from the United States with relatively similar representation from all major geographic areas. A majority of pharmacists participating in the survey were clinical practitioners <5 years (33%) or 5-10 years (29%) removed from their terminal training. These pharmacists most frequently practiced in a medical (30%) or mixed medical/surgical (32%) ICU. Over 90% of pharmacist respondents reported that a pharmacist rounded with the primary or intensivist team at least five days per week.

Vancomycin-related practices in respondent institutions

Practice site characteristics regarding vancomycin are presented in Table 2. The most common responses regarding what percentage of *Staphylococcus aureus* isolates were methicillin-resistant *Staphylococcus aureus* (MRSA) were either 20-39% (23% of respondents) or 40-59% (34% of respondents). Vancomycin was routinely reported as empiric therapy in hospital-acquired infections by 67% of respondents. Fifty-five percent of respondents estimated the average duration of vancomycin use prior to de-escalation when MRSA is not cultured as 48-72 hours. A large majority of respondents (85%) reported that their institution reports the vancomycin minimum inhibitory concentrations for MRSA in the medical record.

Approximately one-third of respondents (31%) reported their institution had no formal pharmacy consult order (or pharmacy to dose protocol) to dose vancomycin. Another 31% of respondents reported that pharmacists may deviate from the protocol as written, which they sometimes do (10-50% of the time). The majority of pharmacists had a protocol or other mechanism in place to order vancomycin serum concentrations (83%), laboratory monitoring (eg. basic metabolic panel) (72%), or dose adjust according to vancomycin serum concentration or renal function (78%); 18% of respondents reported no formal mechanism for placing these orders, requiring they be placed under a provider's name pursuant to a verbal or written order.

Twenty percent of respondents reported a protocol for vancomycin dosing in the setting of CRRT with a mechanism to alert the pharmacist that CRRT is being initiated or discontinued; another 30% have a protocol with no mechanism to alert the pharmacist of CRRT initiation or discontinuation. Most

Table 2. Practice site characteristics and vancomycin-related demographics.

	NUMBER (%)
Institutional Protocol Description and Pharmacist Adherence	
Pharmacists must adhere to the protocol as written and may not deviate	8/364 (2.2)
Pharmacists may deviate from the protocol as written, but I rarely[a] do	36/364 (9.9)
Pharmacists may deviate from the protocol as written, which I sometimes[b] do	111/364 (30.5)
Pharmacists may deviate from the protocol as written, which I often[c] do	63/364 (17.3)
Pharmacists may deviate from the protocol as written, and I routinely[d] do	34/364 (9.3)
No formal protocol exists in my primary practice	112/364 (30.8)
Pharmacist Authorized to Order	
Vancomycin levels	303/364 (83.2)
Laboratory tests for monitoring (eg. basic metabolic panel)	262/364 (72.0)
Dose adjustments based on vancomycin levels or renal function changes	283/364 (77.8)
Institutional Protocol for Vancomycin Dosing in Continuous Renal Replacement Therapy (CRRT)	
Yes; but there is no mechanism to alert the pharmacist that CRRT is being initiated or discontinued	109/364 (29.9)
Yes; and there is a mechanism to alert the pharmacist that CRRT is being initiated or discontinued	71/364 (19.5)
No; and there is no mechanism to alert the pharmacist that CRRT is being initiated or discontinued	93/364 (25.6)
No; but there is a mechanism to alert the pharmacist that CRRT is being initiated or discontinued	51/364 (14.0)
Primary practice ICU does not utilize CRRT	40/364 (11.0)
Institutional Vancomycin Monitoring and Quality Assurance Programs	
Quality assurance for percentage of vancomycin dosing regimens within goal target parameters	96/364 (26.4)
Real-time clinical decision support to notify pharmacists of acute changes in serum creatinine or urine output	90/364 (24.7)
Standardized definition of vancomycin-associated nephrotoxicity	27/364 (7.4)
None of these	159 (43.7)
Estimated Methicillin Resistant *Staphylococcus aureus* Isolates	
20-39%	84/364 (23.1)
40-59%	122/364 (33.5)
60-80%	25/364 (6.9)
Other	32/364 (8.8)
Unknown/No specific antibiogram	101/364 (27.7)
Estimated Frequency of Empiric Vancomycin Therapy for Suspected Hospital-Acquired Infections	
Rarely[a]	6/364 (1.6)
Sometimes[b]	16/364 (4.4)
Often[c]	99/364 (27.2)
Routinely[d]	243/364 (66.8)
Estimated Average Duration of Vancomycin Use Prior to De-escalation when MRSA is Not Cultured	
<2 days (<48 hours)	16/364 (4.4)
2-3 days (48-72 hours)	201/364 (55.2)
3-4 days (72-96 hours)	109/364 (30.0)
>4 days (>96 hours)	38/364 (10.4)

[a]<10% of the time; [b]10-50% of the time; [c]51-90% of the time; [d]>90% of the time.

respondents (60%) did not use sustained low efficiency dialysis (SLED) at their practice site.

When asked which vancomycin monitoring and quality assurance programs were offered at their institutions, respondents indicated low rates of participation with regard to quality assurance for percentage of vancomycin dosing within a goal parameter (26%), clinical decision support to identify acute changes in serum creatinine or urine output (25%), and standardized definition of vancomycin-associated nephrotoxicity (7%).

Respondent vancomycin dosing practices

Complete results are displayed in Table 3. With respect to scenario-based questions regarding use of vancomycin loading doses, responses were mixed across scenarios. The percentage of pharmacists reporting either routinely or often (51-90% of the time) using a loading dose for the surveyed conditions were as follows: meningitis/CNS infection (84%), septic shock (79%), infective endocarditis (75%), pneumonia in a mechanically ventilated patient (69%), sepsis without shock (61%), and pneumonia in a non-mechanically ventilated patient (54%). When respondents were asked why they did not administer a loading dose at times for a critically ill patient, the most common response was that their assessment of the patient did not meet the definition of severely ill (40%), followed by lack of clinical outcome data supporting the loading dose strategy (23%) and nephrotoxicity concerns (20%). Written comments by survey respondents suggested other possible reasons, including physician concerns for nephrotoxicity and logistics of having to compound the loading dose in the pharmacy versus using doses readily available in the patient care area from automated dispensing cabinets.

Over 90% of respondents reported using actual body weight for loading doses and maintenance doses in normal or underweight patients. For overweight or obese patients, 56% of respondents reported using actual body weight (41% used adjusted body weight) for a loading dose and 45% of respondents reported using actual body weight (51% used adjusted body weight) for maintenance dosing. The most commonly reported dose cap for a loading dose was 2,000 mg (45%) followed by 2,500 mg (28%), while 2,000 mg was the most commonly reported dose cap for maintenance dosing with the majority of respondents (75%).

The majority of respondents reported rarely assessing post-loading dose concentrations, two level kinetics following the first dose, and peak levels. The vast majority (87%) of respondents reported using trough values while 13% reported using trough and AUC. When using trough values, 24% of respondents report that doses are held routinely pending evaluation of the level, while 64% report doses are held pending evaluation only in the setting of suspected acute kidney injury.

Pharmacists most commonly (92%) reported administering vancomycin via intermittent infusion with the majority of pharmacists rarely using continuous infusion. Pharmacist perception of their comfort level with AUC calculations was variable with intermittent infusion. The majority of respondents (62%) report being not at all comfortable with AUC calculations for continuous infusions.

In exploratory regression models, respondents from larger hospitals were overall less likely than smaller hospitals to report consistently using loading doses often or routinely in all six scenarios presented: 250-499 beds (OR 0.4, 95% CI 0.2-0.9), 500-750 beds (OR 0.4, 95% CI 0.2-0.9), and >750 beds (OR 0.4, 95% CI 0.2-0.8) [reference hospitals with <250 beds]. Europe (OR 22.8, 95% CI 2.3-228.7) and Western US regions (OR 3.6, 95% CI 1.5-8.6) were more likely to report using AUC as a target pharmacokinetic parameter for vancomycin use. No predictors were identified for reported comfort with AUC calculations.

Discussion

Compliance with clinical practice guidelines is influenced by many factors, notably the quality of the guidelines themselves, users of the guidelines, and implementation context.[8] Critical care pharmacists were overall compliant with many of the 2009 guideline recommendations assessed except for a few particular areas. Specifically, we observed inconsistent use of a loading dose, dosing weight in obese patients, and quality improvement efforts related to systematically monitoring vancomycin-associated nephrotoxicity.

A survey of infectious disease pharmacist self-reported adherence to the 2009 guidelines was previously published in 2013.[3] Key variations in infectious disease pharmacist reported practices from 2009 guideline recommendations involved the recommendations around loading doses in seriously ill patients (only 42% reported always), use of actual body weight to dose obese patients (40% reported sometimes; 52% reported always), and systematically monitoring nephrotoxicity with a standard definition to routinely identify and report vancomycin-associated nephrotoxicity (34% reported never; 35% reported sometimes).[3] The authors of this study noted it imperative to discern reasons for noncompliance to the loading dose recommendation, particularly in severely ill patients who may benefit and have altered pharmacokinetics.[3] Our survey builds on prior work with a larger and more diverse study sample and is unique by focusing on adult critical care pharmacists, includes survey items regarding sources of practice variation related to vancomycin in critically ill patients, and investigates reasons for pharmacists not adhering to certain 2009 guideline recommendations.

Our survey also identified variation in compliance with loading dose recommendations; however, some pharmacists report practicing differently in specific scenarios. In particular, their assessment of severity of illness appears to be a large factor in administering a loading dose. Although some respondents may consider an ICU patient "severely ill" as the 2009 guidelines term it, this classification can be subjective.[1] Lack of clinical outcomes behind the 2009 recommendation for loading doses (IIIB recommendation) and concerns of

Table 3. Vancomycin dosing and monitoring strategies.

FREQUENCY OF LOADING DOSE RECOMMENDATION BY INDICATION				
	RARELY[a]	SOMETIMES[b]	OFTEN[c]	ROUTINELY[d]
Infective endocarditis	52/364 (14.3)	40/364 (11.0)	70/364 (19.2)	202/364 (55.5)
Meningitis/CNS infection	33/364 (9.1)	27/364 (7.4)	54/364 (14.8)	250/364 (68.7)
Pneumonia in a MV patient	51/363 (14.1)	60/363 (16.5)	75/363 (20.7)	177/363 (48.8)
Pneumonia in a non-MV patient	94/363 (25.9)	74/363 (20.4)	71/363 (19.6)	124/363 (34.2)
Sepsis with shock	40/364 (11.0)	38/364 (10.4)	68/364 (18.7)	218/364 (59.9)
Sepsis without shock	67/363 (18.5)	74/363 (20.4)	82/363 (22.6)	140/363 (38.6)
Pharmacist Reasoning When Choosing Not to Administer a Loading Dose				
Lack of clinical outcome data supporting strategy				83/364 (22.8)
Nephrotoxicity concerns				73/364 (20.1)
Time required to infuse				13/364 (3.6)
The patient does not meet my definition of severely ill				146/364 (40.1)
Other				71/364 (19.5)
MOST COMMONLY USED WEIGHT FOR DOSING VANCOMYCIN				
		ACTUAL BODY WEIGHT	IDEAL BODY WEIGHT	ADJUSTED BODY WEIGHT
Loading dose for normal/underweight patients		353/361 (97.8)	5/361 (1.4)	3/361 (0.8)
Loading dose for overweight/obese patients		201/361 (55.7)	12/361 (3.3)	148/361 (41.0)
Maintenance dose for normal/underweight patients		341/361 (94.5)	9/361 (2.5)	11/361 (3.1)
Maintenance dose for overweight/obese patients		162/361 (44.9)	16/361 (4.4)	183/361 (50.7)
MOST COMMONLY USED DOSE CAP				
	2000 MG PER DOSE	2500 MG PER DOSE	3000 MG PER DOSE	>3000 MG PER DOSE	NO CAP/MAX DOSE
Loading dose	164/362 (45.3)	102/362 (28.2)	61/362 (16.9)	8/362 (2.2)	27/362 (7.5)
Maintenance dose	273/362 (75.4)	43/362 (11.9)	10/362 (2.8)	2/362 (0.6)	34/362 (9.4)
USE OF THE FOLLOWING STRATEGIES TO ASSESS VANCOMYCIN EXPOSURE AND CALCULATE FURTHER DOSING				
	RARELY[a]	SOMETIMES[b]	OFTEN[c]	ROUTINELY[d]
Collect a post-loading dose level	322/361 (89.2)	29/361 (8.0)	3/361 (0.8)	7/361 (1.9)
Two-level kinetics after first dose	277/361 (76.7)	63/361 (17.5)	14/361 (3.9)	7/361 (1.9)
Collect peak levels	325/361 (90.0)	21/361 (5.8)	6/361 (1.7)	9/361 (2.5)
Collect trough levels	9/362 (2.5)	18/362 (5.0)	32/362 (8.8)	303/362 (83.7)
Frequency of Doses Held Pending Level Evaluation When Trough Levels are Collected				
Doses are held routinely (>90% of the time) pending level evaluation				87/362 (24.0)
Doses are held pending level evaluation only if kidney injury is suspected or known				233/362 (64.4)
Doses are held rarely (<10% of the time), even if kidney injury is suspected or known				42/362 (11.6)
Target Pharmacokinetic Dosing and Monitoring Parameter				
Trough				314/363 (86.5)
AUC				2/363 (0.6)
Trough and AUC				47/363 (12.9)

(Continued)

Table 3. (Continued)

FREQUENCY OF VANCOMYCIN DOSING VIA METHOD OF ADMINISTRATION				
	RARELY[a]	SOMETIMES[b]	OFTEN[c]	ROUTINELY[d]
Intermittent infusion	10/364 (2.8)	11/364 (3.0)	8/364 (2.2)	335/364 (92.0)
Continuous infusion	342/363 (94.2)	16/363 (4.4)	3/363 (0.8)	2/363 (0.6)
COMFORT LEVEL ASSESSING VANCOMYCIN LEVELS TO CALCULATE AUC				
	NOT AT ALL COMFORTABLE	SOMEWHAT UNCOMFORTABLE	SOMEWHAT COMFORTABLE	EXTREMELY COMFORTABLE
Intermittent infusion	134/363 (36.9)	54/363 (14.9)	100/363 (27.6)	75/363 (20.7)
Continuous infusion	223/362 (61.6)	59/362 (16.3)	49/362 (13.5)	31/362 (8.6)

[a]<10% of the time; [b]10-50% of the time; [c]51-90% of the time; [d]>90% of the time; AUC, area-under-the-curve; CNS, central nervous system; MV, mechanically ventilated.

nephrotoxicity in an already at-risk patient population are also commonly reported reasons for selectively administering loading doses.[1] Concerns of nephrotoxicity with loading doses by physician colleagues were also noted in the written responses from pharmacist respondents in this survey and identified as potential barriers to routinely using loading doses.

There were similar discrepancies between using actual body weight for dosing in obese patients between the two surveys, with a number of pharmacists in the current survey reporting use of an adjusted body weight.[3] The pharmacokinetics of vancomycin are known to be an area of controversy in obese patients.[9] Due to the hydrophilicity of vancomycin and the increase in adipose tissue associated with obesity, its volume of distribution is somewhat increased in obese patients. In addition, various dosing weights, including ideal body weight, total body weight, and adjusted body weight, have been evaluated in estimating clearance of vancomycin with conflicting results.[10] Given the complexity of critically ill, obese patients and a lack of strong evidence for how to optimally dose vancomycin in these patients, it is not surprising that our survey revealed such practice variation.

In both our survey and that of Davis et al.,[3] there do seem to be opportunities related to standardized definitions of vancomycin-associated nephrotoxicity and quality improvement programs to track and monitor this complication.[3] The possibility exists that this is done within the context of antimicrobial stewardship programs and surveyed ICU pharmacists may not be aware, but this was reported as similarly low in the survey of infectious diseases pharmacists.[3] Additionally, an opportunity may exist for more institutions to implement CRRT alert triggers for pharmacists to increase or decrease doses, as appropriate.

The majority of critical care pharmacists surveyed rarely employed continuous infusion dosing of vancomycin. Interestingly, recent evidence suggests that continuous infusions may be less nephrotoxic than intermittent infusions, particularly in critically ill patients.[11-13] Of paradoxical interest is that pharmacists were reportedly far less comfortable with AUC calculations for continuous infusions than with intermittent infusions, given the AUC calculations for continuous infusion are much simpler than for intermittent dosing. The varying comfort level with AUC calculations in this survey demonstrates the importance of educational efforts that will be needed to employ AUC-guided dosing in ICU patients on a larger scale, as is recommended by the revised vancomycin consensus guidelines recently published in May of 2020.[14]

Our exploratory analysis found that respondents from larger hospitals were generally less likely to report consistent use of loading doses compared to respondents from hospitals with <250 beds. While the exact reasoning for this is unknown, it could be due to a relatively smaller number of respondents from hospitals with <250 beds (15.1% of respondents) or perhaps improved compliance with protocols and guideline recommendations in smaller hospitals from this survey. Additionally, our analysis suggests geographic variation in early adoption of AUC to guide vancomycin dosing, with greater adoption in Western United States and Europe at the time our survey was administered. Pharmacist education is clearly required for AUC dosing and monitoring given the reported comfort rates. Although the pharmacokinetic assumptions are fewer and calculations easier with continuous infusion, this may simply represent the unfamiliarity of critical care pharmacists surveyed with employing continuous infusions due to the low frequency of use identified.

Our study has important limitations to acknowledge. Only SCCM CPP members participated in the study; thus, reported behaviors from non-survey responders and non-SCCM CPP members may be different. This survey only inquired about self-reported actions regarding vancomycin and may not reflect actual actions from clinicians in their practice. Multiple respondents may have responded from the same institution, thus biasing some reported metrics. Our response rate of 26% limited the number of respondents that we were able to collect data from, however, our study is more than twice as large as the prior study of vancomycin dosing practices.[3] Although Europe was identified as using AUC more than others in this survey, there were few respondents from Europe, which may only represent a few institutions and not be representative of European practice. Finally, our survey was disseminated in the spring of 2017, and we suspect additional centers have transitioned to AUC

Table 4. Comparisons between 2009 and 2020 vancomycin consensus guidelines relevant to survey of dosing practices.

DOSING CONSIDERATION	2009 VANCOMYCIN GUIDELINES[1]	2020 REVISED CONSENSUS GUIDELINES[14]
Monitoring Parameters	"Trough serum vancomycin concentrations are the most accurate and practical method for monitoring vancomycin effectiveness." (IIB)	"Trough-only monitoring, with a target of 15-20 mg/L, is no longer recommended based on efficacy and nephrotoxicity data in patients with serious infections due to MRSA" (A-II) "In patients with suspected or definitive serious MRSA infections, an individualized target of the AUC/MIC ratio of 400-600 (assuming a vancomycin MIC of 1 mg/L) should be advocated to achieve clinical efficacy while improving patient safety." (A-II)
Loading Dose and Weight	"In seriously ill patients, a loading dose of 25-30 mg/kg (based on actual body weight) can be used to facilitate rapid attainment of target trough serum vancomycin concentration." (IIIB)	"In order to achieve rapid attainment of targeted concentrations in critically ill patients with suspected or documented serious MRSA infections, a loading dose of 20-35 mg/kg can be considered for intermittent-infusion administration of vancomycin." (B-II) "Loading doses should be based on actual body weight and not exceed 3000 mg. More intensive and early therapeutic drug monitoring should also be performed in obese patients." (B-II)
Maintenance Dosing Weight	"Vancomycin dosages should be calculated on actual body weight. For obese patients, initial dosing can be based on actual body weight and then adjusted based on serum vancomycin concentrations to achieve therapeutic levels." (IIA)	"Initial maintenance doses of vancomycin can be computed using a population pharmacokinetic estimate of vancomycin clearance and the target AUC in obese patients. Empiric maintenance doses for most obese patients usually do not exceed 4500 mg/day, depending on their renal function." (B-II)
Continuous Infusion	"Continuous infusion regimens are unlikely to substantially improve patient outcome when compared with intermittent dosing." (IIA)	"The pharmacokinetics of continuous infusion suggest that such regimens may be a reasonable alternative to conventional intermittent-infusion dosing when the AUC target cannot be achieved." (B-II)

monitoring at this time given a signal of increased safety in terms of kidney injury as well as anticipated (and actual) endorsement of AUC guided dosing in recently released revised consensus vancomycin guidelines.[14-16] Although these revised guidelines have been published since our survey, aside from recommending a change from trough-based dosing to AUC and no longer directly recommending actual body weight in maintenance dosing for obesity, many of the recommendations as they relate to our survey remain similar between the 2009 and 2020 guidelines.[1,14] Table 4 compares relevant dosing considerations from our survey between the 2009 and 2020 guidelines.[1,14] Our data may serve as a benchmark in evaluating uptake of consensus guideline recommendations, particularly against the backdrop of showing a relatively low "early-adopter" rate for AUC-guided dosing. In the context of newly revised consensus guidelines, we also show continued room for improvement with the guideline recommendation for loading doses, and demonstrate that a small percentage of surveyed pharmacists are employing continuous infusion. Finally, our survey also establishes the prevalence of important dosing concepts that may not be presented as formal guideline recommendations yet may reflect best practices in dosing vancomycin in critically ill patients, including electronic alerts for CRRT initiation or discontinuation.

Conclusion

Critical care pharmacists' reported practices regarding vancomycin are largely consistent with the 2009 vancomycin guideline recommendations. Important areas of variation include use of loading doses, dosing weights in obese patients, and quality improvement efforts related to systematically monitoring vancomycin-associated nephrotoxicity. Further study in these particular areas may allow more definitive guideline recommendations to help optimize vancomycin use in the critically ill.

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Author Contributions

AF is responsible for conception, analysis, and drafting the initial manuscript. CL is responsible for statistical analysis. DH, DO, CL, AW, AS, QMY, WC, CP, APR, PJ contributed to survey development and manuscript revision.

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Supplemental material

Supplemental material for this article is available online.

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