Medication regimen complexity vs patient acuity for predicting critical care pharmacist interventions

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Purpose. Quantifying and predicting critical care pharmacist (CCP) workload has significant ramifications for expanding CCP services that improve patient outcomes. Medication regimen complexity has been proposed as an objective, pharmacist-oriented metric that demonstrates relationships to patient outcomes and pharmacist interventions. The purpose of this evaluation was to compare the relationship of medication regimen complexity versus a traditional patient acuity metric for evaluating pharmacist interventions.

Summary. This was a post hoc analysis of a previously completed prospective, observational study. Pharmacist interventions were prospectively collected and tabulated at 24 hours, 48 hours, and intensive care unit (ICU) discharge, and the electronic medical record was reviewed to collect patient demographics, medication data, and outcomes. The primary outcome was the relationship between medication regimen complexity–intensive care unit (MRC-ICU) score, Acute Physiology and Chronic Health Evaluation (APACHE) II score, and pharmacist interventions at 24 hours, 48 hours, and ICU discharge. These relationships were determined by Spearman rank-order correlation (r_S) and confirmed by calculating the beta coefficient (β) via multiple linear regression adjusting for patient age, gender, and admission type. Data on 100 patients admitted to a mixed medical/surgical ICU were retrospectively evaluated. Both MRC-ICU and APACHE II scores were correlated with ICU interventions at all 3 time points (at 24 hours, $r_S = 0.370$ [$P < 0.001$] for MRC-ICU score and $r_S = 0.283$ [$P = 0.004$] for APACHE II score); however, this relationship was not sustained for APACHE II in the adjusted analysis (at 24 hours, β = 0.099 [$P = 0.001$] for MRC-ICU and β = 0.031 [$P = 0.085$] for APACHE II score).

Conclusion. A pharmacist-oriented score had a stronger relationship with pharmacist interventions as compared to patient acuity. As pharmacists have demonstrated value across the continuum of patient care, these findings support that pharmacist-oriented workload predictions require tailored metrics, beyond that of patient acuity.

Keywords: critical care, drug-drug interactions, patient acuity, patient safety, pharmacy practice models

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Predicting intensive care unit (ICU) clinician workload is established in other professions, but only preliminary work has begun with critical care pharmacists (CCPs).[1,2] In particular, among ICU nurses significant decreases in mortality have been demonstrated when the nurse-to-patient ratio is reduced.[3-5] Further, the profession of nursing has developed numerous scores to predict the amount of nursing care a particular ICU patient requires, including the Nursing Activities Score (NAS) and Therapeutic Intervention Scoring System (TISS-28).[6,7] While these scores have imperfect agreement amongst each other and often capture different elements of the more holistic concept of workload in the ICU, they provide a construct for adaptation to critical care

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pharmacy practice, which is in need of similar optimization efforts.[8]

CCPs improve patient-centered outcomes and enhance medication safety, all while reducing healthcare costs.[9-13] As such, CCPs are recognized as essential members of the ICU team by organizations representing both pharmacy and nonpharmacy healthcare providers.[14-16] Despite this strong evidence and interprofessional support, recent assessments have demonstrated CCPs are an underused, inequitably distributed healthcare resource that is unavailable to all Americans.[17-19] Moreover, despite knowledge that the ratio of healthcare workers to patients directly relates to mortality, no such studies for pharmacists have been undertaken. It is notable that strikingly few institutions provide 24/7/365 CCP coverage, even during a global pandemic that stretched ICU resources to the maximum,[18,20,21] and that guidelines make no reference to optimal CCP-to-patient ratios.[14,22,23]

Appropriate staffing models and tools to prioritize CCP workload are important to optimize the efficacy and efficiency of this resource in order to both improve patient outcomes and reduce the risk of burnout, which is prevalent among CCPs.[24,25] Prioritization tools should be used not only at the bedside to prioritize care but also to help define optimal CCP-to-patient ratios, which vary widely in current practice.[18]

As traditional patient acuity scores like the Acute Physiology and Chronic Health Evaluation (APACHE) II score are widely recognized, extensively validated, and often available in the electronic medical record, these scores have also been included during decision-making with regard to ICU clinician-to-patient ratios.[26] However, the intention of these scores was never workload oriented, and they are not established in other professions for this use.[2] The complex interplay among clinician staffing levels, communication between clinicians, patient preferences, technology, work processes, and clinical outcomes is important in assessing staffing models and is not taken into account when calculating patient acuity scores designed to predict ICU mortality.[27] To date, the only metric that has been specifically designed or validated for CCPs is the medication regimen complexity–intensive care unit (MRC-ICU) scoring tool. This objective tool provides a quantitative score of a patient's medication regimen complexity.[28] In turn, this score has been correlated with mortality, ICU length of stay, drug-drug interactions, fluid overload, and pharmacist interventions.[28-33]

The purpose of this study was to evaluate the correlation of the MRC-ICU scoring tool versus a traditional patient acuity score (APACHE II score) with pharmacist workload, as measured by pharmacist interventions. As clinical pharmacists are well established throughout the continuum of care (ie, regardless of patient acuity), we hypothesized that a CCP-oriented metric would have superior correlation to CCP workload.

KEY POINTS

- Quantifying and predicting critical care pharmacist workload is important for expanding pharmacy services that improve patient outcomes.
- In a retrospective post hoc analysis, the medication regimen complexity–intensive care unit (MRC-ICU) score had a stronger relationship with pharmacist interventions and drug-drug interactions than a traditional patient acuity score.
- The MRC-ICU score may have utility in predicting pharmacist interventions and potential medical safety events.

Study methodology

This study was a post hoc analysis of a multicenter, prospective, observational study. Institutional review board approval was obtained from both participating sites. Adult patients admitted to the mixed medical/surgical ICU from March through May 2018 at Piedmont Athens Regional were enrolled. Patients with an ICU length of stay less than 24 hours or active hospice orders were excluded. Patients admitted to the second center (Augusta University Medical Center) were not included in this post hoc analysis, as the APACHE II score was not available for this subgroup. Data points collected included the MRC-ICU score calculated at 24 hours after ICU admission; demographic data including age, gender, race, and APACHE II score; the number of pharmacist interventions at 24 hours, 48 hours, and ICU discharge; and the number of drug-drug interactions at 24 hours. The full study details have been published previously.[33]

The primary outcome was to compare the relationship between patient acuity, as measured by the APACHE II score, and medication complexity, as measured by the MRC-ICU score, with the number of pharmacist interventions at 24 hours, 48 hours, and ICU discharge. The secondary outcome was to compare the relationship between APACHE II and MRC-ICU scores with the number and categories of drug-drug interactions (DDIs) at 24 hours.

Statistical analyses were completed using IBM SPSS Statistics for Windows, Version 26 (IBM Corporation, Armonk, NY). Descriptive statistics were calculated for all variables and were reported as number and percentage or median and interquartile range (IQR). The primary and secondary outcomes were assessed using 2 methodologies. First, Spearman rank order correlation was used to determine the correlation between APACHE II and MRC-ICU scores and number of pharmacist interventions and DDIs. The Spearman rank-order correlation was selected, as data were determined to fit a nonparametric distribution. Second, adjusted analyses were performed by developing multiple linear regression models to determine the relationship between APACHE II and MRC-ICU scores and number of pharmacist interventions

and drug-drug interactions when controlling for patient age, gender, and type of ICU admission (medical versus surgical). For both methodologies, correlation coefficients and beta coefficients, respectively, were compared visually for the APACHE II and MRC-ICU scores. For all analyses, an α of <0.05 was considered significant.

Results

A total of 100 patients were included, 50 medical admissions and 50 surgical admissions. The median MRC-ICU score at 24 hours of ICU admission was 11 (IQR, 8-14), and the median APACHE II score at ICU admission was 18 (IQR, 11-24). There was a median of 2 (IQR, 1-5) pharmacist interventions documented per patient during the ICU stay and a median of 28 (IQR. 18-55) potential DDIs identified within 24 hours of ICU admission. Baseline characteristics, number of interventions at each time point, number and type of DDIs, and patient outcomes are summarized in Table 1.

APACHE II score was correlated with the number of pharmacist interventions at 24 hours, 48 hours, and ICU discharge; however, this relationship was lost in the adjusted analysis accounting for potentially confounding variables including patient age, gender, and admission type (medical vs surgical) (Table 2, eFigure 1). MRC-ICU score was correlated with the number of pharmacist interventions at each time point, and this relationship remained true in the adjusted analyses (eFigure 2). APACHE II score was not associated with DDIs in either analysis, whereas MRC-ICU score was associated with the number of DDIs in each category except for category X DDIs.

Discussion

This evaluation is to our knowledge the first to demonstrate that both patient acuity and medication regimen complexity are associated with pharmacist workload, as measured by pharmacist interventions. Notably, a metric designed to capture medication regimen complexity (and the associated management of high-risk medications) had a stronger relationship than the traditional acuity metric (APACHE II score).

While MRC-ICU score had a stronger correlation with pharmacist workload than APACHE II score, the difference was not substantially higher, indicating that combinations of acuity, medication regimen complexity, and other patient data may ultimately be a better marker for pharmacist workload. This combination of medication-related and patient-acuity information improving predictions has been observed with previous evaluations of the MRC-ICU, wherein application of machine-learning to APACHE III and MRC-ICU demonstrated improved mortality predictions.[31] APACHE II score did not relate to DDI, supporting the widely accepted belief that pharmacist review of medications is needed regardless of patient acuity (eg, from the community through ICU setting) and that development of pharmacist-oriented metrics may yield novel insights.[34,35]

The construct of objective metrics used for comparison and forecasting is well established in critical care (though much work is yet to be done).[2,36] Indeed, in a recent review of the history of severity-of-illness indicators and their use in predictive models, Kramer et al[2] detailed the need for "metrics that transcended subjective assessments" in order to draw meaningful conclusions from comparative trials. In this manner, an objective metric with validated external validity that reflects key domains of CCP workload (eg, patient outcomes, medication-related costs, CCP well-being, and other institutional resources) is appealing for the evidence-based development and evaluation of robust CCP practice models, and a recent survey evaluating metrics that measure value and productivity among CCPs showed significant gaps in both institution-level tracking and the ability

Table 1. Baseline Characteristics and Patient Outcomes

Variable	Value (*n* = 100)[a]
Age, y	65 (54-75)
Male gender	46 (46)
Admission weight, kg	74 (62-97)
APACHE II score	18 (11-24)
MRC-ICU score	11 (8-14)
No. of pharmacist interventions	
Within 24 hours of ICU admission	1 (0-2)
Within 48 hours of ICU admission	1 (0-3)
At time of ICU discharge	2 (1-5)
No. of drug-drug interactions at 24 hours	
Class B	5 (3-7)
Class C	15 (6-24)
Class D	7 (2-17)
Class X	0 (0-1)
Total	28 (18-55)
Length of ICU stay, d	2 (2-5)
Inpatient mortality	14 (14)

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; MRC-ICU, medication regimen complexity–intensive care unit.
[a]Data are presented as number (percentage) or median (interquartile range).

Table 2. Relationship of APACHE II Score, MRC-ICU Score, and Patient Outcomes

	APACHE II Score				MRC-ICU Score			
Variable	Correlation Coefficient[a]	*P* Value	β[b]	*P* Value	Correlation coefficient[a]	*P* Value	β[b]	*P* Value
Pharmacist interventions								
At 24 hours	0.283	0.004	0.031	0.085	0.370	<0.001	0.099	0.001
At 48 hours	0.325	0.008	0.037	0.164	0.280	0.023	0.112	0.013
At ICU discharge	0.366	<0.001	0.156	0.001	0.479	<0.001	0.323	<0.001
Drug-drug interactions								
Class B	–0.168	0.243	–0.033	0.607	0.318	0.024	0.312	0.013
Class C	–0.023	0.875	–0.187	0.461	0.383	0.006	1.528	0.002
Class D	–0.331	0.019	–0.358	0.091	0.427	0.002	1.392	0.001
Class X	0.097	0.502	0.025	0.483	0.067	0.646	0.091	0.197
Total	–0.192	0.181	–0.585	0.216	0.452	0.001	3.264	<0.001

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; MRC-ICU, medication regimen complexity–intensive care unit.
[a]Spearman rank-order correlation.
[b]Calculated via multiple linear regression adjusting for age, gender, and admission type (medical vs surgical)

to compare among institutions.[1,37] However, Kramer et al also noted that the development of these metrics was often "more melodrama than scientific debate." As such, even extremely established metrics such as APACHE II may be subject to "model fade" (which may be seen as overprediction of an outcome like mortality as care advances), and other models risk being overspecific to the population studied in their development (that is why, eg, the Simplified Acute Physiology Score [SAPS II] is likely best applied to the European population of its origin).[38] Thus, the *concept* of MRC-ICU is perhaps the most appealing, while much is yet to be done to avoid the traps of model fade, population overfitting, inability to apply analytics in a clinical setting, or other issues of metrics-based evaluation.[2,39] Ultimately, the utility of such a metric is how it can be embedded into clinical decision support systems and other systems that rely on real-time, artificial intelligence–based programming to create meaningful alerts to clinicians.[2]

Multiple studies have proven nurse workload and patient outcome indicators are positively correlated. Margadant et al[40] determined nursing workload is positively associated with in-hospital mortality. Lee et al[3] observed that 1 day of high workload substantially increased the risk of death in ICU patients. Lui et al[41] found a positive correlation between nurse workload and nurse-sensitive patient safety outcomes, including patient falls, decubitus/pressure ulcers, medication errors, unplanned extubations, and hospital-acquired infections. In the same light, this study begins to evaluate the relationship between pharmacist workload and patient outcomes.

This study is limited by its post hoc, observational design that precludes the ability to make inferences regarding the true relationship of medication regimen complexity and patient acuity to pharmacist interventions; however, the results appear hypothesis generating, with important applications to the field of critical care pharmacy.

Conclusion

MRC-ICU score had a stronger relationship with pharmacist interventions than a patient acuity metric and therefore may have future utility as a metric for predicting pharmacist interventions and potential medication safety events. The ability to objectively describe and plan needed CCP resources in the ICU is increasingly important not only to improve patient outcomes but to mitigate the effects of burnout.

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